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Award Number: W81XWH-04-1-0528

TITLE: Relationship of Neurocognitive Function to Breast Cancer Treatment and Induced Menopause

PRINCIPAL INVESTIGATOR: Amy L. Kenefick, Ph.D.

CONTRACTING ORGANIZATION: University of Connecticut
Storrs, CT 06269-2026

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14. ABSTRACT

The intent of this Clinical Research Nurse Award was to facilitate the preparation of the investigator for an active career in collaborative clinical breast cancer research. The training component of this award included formal and informal experiences related to breast cancer research/treatment and research methodology. A nine month longitudinal research study describing changes in neurocognitive function in women receiving chemotherapy for breast cancer and in a comparison group of women having had surgically induced menopause was designed and initiated but a sufficient sample has not yet accrued during the period of this grant.

15. SUBJECT TERMS
Cognition, menopause, symptoms, quality of life

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INTRODUCTION: The intent of this Clinical Research Nurse Award was to facilitate the preparation of the investigator for an active career in collaborative clinical breast cancer research. The training component of this award included formal and informal experiences related to breast cancer research/treatment and research methodology. The research component included the design and execution of a nine-month, longitudinal, repeated measures, descriptive study of neurocognitive function (NCF) in a group of women receiving chemotherapy for breast cancer.

BODY: The statement of work included both research and training goals. These will be discussed individually, below.

Research goals

The research goals included design and execution of a nine month longitudinal research study describing changes in neurocognitive function in women receiving chemotherapy for breast cancer and in a comparison group of women having had surgically induced menopause. The study was designed and we identified two clinical sites suitable for data collection, negotiated collaborative arrangements, and obtained human subjects approval from a total of four Institutional Review Boards.

The data management and analysis plan was designed in collaboration with the statistician. The analysis was designed to determine characteristics of NCF before, during, and after chemotherapy and surgically induced menopause; the longitudinal relationship of NCF and chemotherapy; the relationship between induced menopause and NCF; the nature, severity, onset, duration, and persistence of NCF changes in women who experience menopause induced by breast cancer chemotherapy compared to those experienced by women who have surgically induced menopause; relationships that exist between NCF, symptom distress, and functional status in women before, during, and after chemotherapy.

The subject of instrumentation for the measurement of NCF was discussed at length with two research psychologists. A doctoral student in nursing was hired as research assistant. She received expert training on the proper administration of the subtests of the Wechsler Adult Intelligence Scale by an experienced educational psychologist. A doctoral student in psychology was also engaged to do testing.

We were aware of the difficulties inherent in longitudinal research and planned carefully and proactively for subject recruitment and retention. The research assistant conducted a thorough review of the literature on recruitment and retention. HIPAA Regulations prohibit researchers from direct contact with potential participants in the healthcare facility, therefore it was important for the researcher to be in frequent contact with the clinicians in order for the clinician to be a conduit to participant access. Clinicians have a pivotal role in successful recruitment. Research staff met repeatedly with clinicians providing care to prospective subjects. Mutually acceptable plans were devised. Careful consideration was given to relationship building with all clinicians. Our collaborative accrual and retention plans included clarity in description of the protocol to the subject; interviews at the convenience of the subject; being respectful and valuing

the subject's and the clinician's contributions; allowing for rest periods; providing an incentive grocery certificate; maintaining consistency of data collector; maintaining communication with subjects throughout the study; making thank-you calls after each session; and sending thank-you cards. We consulted repeatedly with experienced researchers who had expertise in longitudinal designs, breast cancer, and clinical trials. Recruitment of subjects proved to be an insurmountable challenge. To our great dismay, we were able to recruit only one subject and she withdrew from the study before the second data collection point.

This research project had significant feasibility issues. They included: the considerable length of time necessary for passing through multiple IRBs; research burden on potential subjects; lack of ability to pay the clinical site for referring subjects; and turnover of staff which interfered with relationship building and maintenance. Extreme delay in securing IRB approval occurred repeatedly. Turnover of personnel and inadequate numbers of personnel in the IRB were cited as the reasons for these delays. While we were able to stimulate excitement among both clinicians and potential subjects about the project, there was a lack of institutional champions to support research. Research was an unfunded add-on to clinician responsibilities and we could not buy their release time. We offered continuing education programs and authorship to those who were interested. Others involved in clinical research in these sites also reported difficulty in accruing subjects for breast cancer research. Reasons cited included too many competitive research projects on breast cancer; lack of interest by patients and clinicians in non-therapeutic studies; inability of patients to consider research participation while they were experiencing the stress of diagnosis and initiation of treatment. In addition, our experience demonstrates the emergence of barriers that have not been identified in the literature, dense-dose therapy with considerable symptom burden and the initiation of therapy within 72 hours of diagnosis.

The project continues to be approved at both sites and we are in the process of reviewing its feasibility.

Training goals

The training aspect of the project was much more successful. Training activities have included attending conferences and interdisciplinary meetings, presenting original research, writing papers based on research done with the mentor, attending classes and doing independent reading related to the design and management of longitudinal research and clinical trials, particularly in breast cancer. As a result of activities associated with this grant (see appendix for curriculum vitae), the investigator, a post-doctoral fellow and assistant professor at the time of application, received tenure, promotion and a joint appointment to the faculty of the schools of nursing and medicine. She has become part of an interdisciplinary team of scientists who are studying breast cancer. She has received funding for translational projects that will be done in breast cancer survivorship (see appendix for award letter); presented and published her research on symptoms in breast cancer; supervised a doctoral student in developing an instrument to measure distress related to NCF changes in women undergoing breast

cancer chemotherapy; served dissertation chair for a student who has conducted a phenomenological study of the same topic; and taken on a lead role in the teaching of statistics to master's students as a result of her classes. In addition, she is a co-investigator in a funded interdisciplinary breast cancer research project that also includes basic scientists, oncologists, a psychiatrist, and a psychologist (see appendix: Mental and Physical Stressors in the Diagnosis of Breast Cancer). Her published work has been cited at least nineteen times by other breast cancer researchers.

KEY RESEARCH ACCOMPLISHMENTS:

The investigator received training in design and analysis of longitudinal research in breast cancer. She has published her research and been funded for interdisciplinary and translational research projects derived from the activities funded in this grant. A nine month longitudinal research study describing changes in neurocognitive function in women receiving chemotherapy for breast cancer and in a comparison group of women having had surgically induced menopause was designed and initiated but a sufficient sample did not accrue during the period of this grant.

REPORTABLE OUTCOMES:

Completed courses

PSYC 507 01 Health Psychology: Clinical and Social Foundations. Introduction to theory and empirical approaches in health psychology. Consideration of the role of psychological variables in the etiology and treatment of disease and in the maintenance of health. Emphasis is placed on current basic research in selected areas of health psychology and on the application of this knowledge base to health care delivery.

BIS 625 01 Categorical Data Analysis. This course presents methods for analyzing categorical data in public health, epidemiology, and medicine. Topics include discrete distributions, log-linear models, and logistic regression. Emphasis is placed on the application of the methods and the interpretation of results by applying the techniques to a variety of data sets.

BIS 628 01 Longitudinal Data Analysis This course covers methods for analyzing data in which repeated measures have been obtained for individuals over time. Different methods are discussed to handle both continuous and discrete longitudinal response data. Both subject-specific and population-averaged approaches are covered (with particular reference to capturing the heterogeneity between different individuals). Some of the approaches covered include linear, nonlinear, and generalized mixed effects models, as well as generalized estimating equations. The course also covers exploratory methods, approaches for handling missing data, and possibly transition models and advanced topics such as multivariate longitudinal responses, nonparametric longitudinal responses, the joint consideration of longitudinal and survival data, and the joint consideration of longitudinal and spatial data. Emphasis is placed on applying the methods, understanding underlying assumptions, and interpreting results.

BIS 561 01 Advanced Topics and Case Studies in Multicenter Clinical Trials. This course addresses advanced issues related to the design, conduct, monitoring, and analysis of multicenter randomized clinical trials. Topics include organizational, regulatory, and human rights issues; an overview of design strategies; advanced topics in sample size estimation and monitoring; data management and quality assurance procedures; cost-effectiveness and quality of life; and case studies of vaccine trials, factorial trials, primary and secondary prevention trials, large simple trials, strategy trials, and cost-effectiveness. The case studies include many of the classical and landmark clinical trials, such as the polio vaccine ?eld trial, Physicians Health Study, and the trials of AZT for the treatment of AIDS.

Abstracts

Kenefick, A. L. (2005). Relationship of neurocognitive function to breast cancer treatment and induced menopause, abstract published in Proceedings of Era of Hope, Department of Defense Breast Cancer Research Program Meeting, 99.

Kenefick, A. (2005). Patterns of symptom distress in elderly women with breast cancer, Virginia Henderson International Library, http://www.nursinglibrary.org

Manuscripts

Kenefick, A.L. and McCorkle, R. (in preparation) Functional outcomes in older women after surgical treatment for breast cancer.

Kenefick, A.L., Swinney, J., and McCorkle, R. (in preparation). Racial disparity in symptom distress following breast cancer surgery.

Jones, B.A., Kenefick, A. L., Zinggeler, J. M., Dubrow, R., and Kasl, S.V. (under review). Delay, race, and breast cancer stage at diagnosis.

Publications

Kenefick, A.L., Schulman-Green, D., McCorkle, R. (2006). Decision-making in pain management using the model of sequential trials. *Alzheimer's Care Quarterly*, *7*(3):175-183.

Kenefick, A.L. (2006). Patterns of symptom distress in older women after surgical treatment for breast cancer. *Oncology Nursing Forum, 33*(2):327-336.

Kenefick, A. L. (2005). Relationship of neurocognitive function to breast cancer treatment and induced menopause, abstract published in Proceedings of Era of Hope, Department of Defense Breast Cancer Research Program Meeting, 99.

Kenefick, A.L. and Schulman-Green D. (2004). Caring for cognitively impaired nursing home residents within. pain. *International Journal of Human Caring, 8*(2): 32-40.

Kenefick, A.L. (2004). Pain Treatment and Quality of Life: Reducing Depression and Improving Cognitive Impairment. *Journal of Gerontological Nursing, 30*(5): 22-29.

Chen, C., Kenefick, A., Tang, S.T., McCorkle, R. (2004). Utilization of comprehensive geriatric assessment in cancer patients. *Critical Reviews in Oncology and Hematology, 49*(1): 53-67.

Presentations

Functional Dependency of Older Women After Breast Cancer Surgery, 9th National

Conference on Cancer Nursing Research, Hollywood California, February 10, 2007.

Neurocognitive Symptoms in Patients with Cancer, Yale School of Nursing, January 8, 2007.

Participatory Research in Breast Cancer Survivorship, The Carole and Ray Neag Comprehensive Cancer Program: Third Annual Research Retreat, Water's Edge Resort & Spa, Westbrook, CT, 11/27/2006

Cognitive Changes in Patients with Cancer, Yale University School of Nursing, April 4, 2006.

Quality of Life Assessment in Cancer Clinical Trials, The Carole and Ray Neag Comprehensive Cancer Program: Second Annual Research Retreat, Water's Edge Resort & Spa, Westbrook, CT, 11/5/2005

Researching Symptom Experience Following Surgical Treatment of Breast Cancer, University of Connecticut Health Center, 5/19/2005

Patterns of Symptom Distress in Elderly Women with Breast Cancer. Poster, Distinguished Scholars Day, University of Connecticut, 4/14/ 2005

Patterns of Symptom Distress in Elderly Women with Breast Cancer. Paper, 17th Annual Scientific Sessions of the Eastern Nursing Research Society, 4/8/ 2005

Relationship of Neurocognitive Function to Breast Cancer Treatment and Induced Menopause, Neag Comprehensive Cancer Program, University of Connecticut Health Center, 12/16/ 2004

Innovative Program of Research in Breast Cancer, University of Connecticut School of Nursing Advisory Board and UConn Foundation, 10/1/ 2004

Questioning the Information on Delay and Racial Disparities in Breast Cancer Survival, Paper, Association of Women's Health, Obstetric and Neonatal Nurses Annual Convention, "Challenging the Status Quo" , 6/29/ 2004

Blaming the Victim? Blaming the System? The Relationship of Delay to Stage of Disease at th Time of Breast Cancer Diagnosis, Poster, Scholars' Day, University of Connecticut, 4/22/ 2004

Delay and Racial Disparity in Stage at Diagnosis in Women with Breast Cancer, Paper, 16th Annual Scientific Sessions of the Eastern Nursing Research Society, 4/3/2004

Grants funded based on work supported by this award

Mental and Physical Stressors in the Diagnosis of Breast Cancer: A multidisciplinary analysis of stress and systemic biomarkers in patients referred for biopsy of a suspected breast cancer lesion	The Connecticut Breast Health Initiative		2006-2007	$75,000	Co-Investigator
Translational Research in Breast Cancer Survivorship	University of Connecticut	Pauline A. Toner Fund	2006	$5,000	PI

Employment or research opportunities applied for and/or received based on experience/training supported by this award.

Granted joint appointment as Assistant Professor, School of Medicine, University of Connecticut

Member, American Cancer Society Institutional Grant Review Board UCONN Health Center
Member, Intercampus Interdisciplinary Oncology Program Steering Committee
UCONN Health Center Breast Cancer Research Cooperative, 2005- present

CONCLUSION:

The investigator received training in design and analysis of longitudinal research in breast cancer. She has published her research and been funded for interdisciplinary and translational research projects derived from the activities funded in this grant. A nine month longitudinal research study describing changes in neurocognitive function in women receiving chemotherapy for breast cancer and in a comparison group of women having had surgically induced menopause was designed and initiated but a sufficient sample did not accrue during the period of this grant. This research project had significant feasibility issues. They included: the considerable length of time necessary for passing through multiple IRBs; research burden on potential subjects; lack of ability to pay the clinical site for referring subjects; and turnover of staff which interfered with the relationship building and maintenance necessary for the project to succeed. Understanding cognitive impairment associated with chemotherapy for breast cancer continues to be a problem in both research and clinical practice. This is largely due to issues of instrumentation and study design. Research continues to show small to moderate effect sizes that vary depending on the type of design used. Practice effect is noted and there is poor correlation between patients' perception of their cognitive impairment and objective testing.

REFERENCES:

None

APPENDICES:

Curriculum vitae
Patterns of Symptom Distress in Older Women after Surgical Treatment for Breast Cancer
Decision Making in Pain Management Using the Model of Sequential Trials
Utilization of Comprehensive Geriatric Assessment in Cancer Patients
Faculty appointment, School of Medicine, University of Connecticut
Award letter, Translational Research in Breast Cancer Survivorship
Relationship of Neurocognitive Function to Breast Cancer Treatment and Induced Menopause, abstract for DOD breast cancer meeting
Mental and Physical Stressors in the Diagnosis of Breast Cancer: A Multidisciplinary Analysis of Distress and Systemic Biomarkers in Patients Referred for Biopsy of a Suspected Breast Cancer Lesion, protocol summary

SUPPORTING DATA:

None

Amy Laufer Kenefick, PhD, APRN,BC

Associate Professor, School of Nursing
Assistant Professor, School of Medicine
University of Connecticut
Storrs, CT 06269-3044
amy.kenefick@uconn.edu

EDUCATION

BA, Demography. University of Massachusetts at Amherst, 1975
BSN, Nursing, Cornell University, New York, 1977.
MSN, Nursing, University of Kentucky, Lexington, 1981.
PhD, Nursing, University of Massachusetts at Amherst and Worcester, 1999.
Postdoctoral Fellowship. School of Nursing, Yale University, 2002-2003
Special Student, Epidemiology and Public Health, School of Medicine, Yale University, 2005-2006
Special Student, Psychology, Yale University, 2006-2007

RESEARCH AND TEACHING INTERESTS

Quality of life outcomes in clinical trials, breast cancer, advanced practice nursing, nursing theory

LICENSURE AND CERTIFICATION

CT: Registered Nurse, Advanced Practice Registered Nurse
MA: Registered Nurse/Midwife, Registered Nurse/Practitioner
Certified Nurse Midwife, American College of Nurse Midwives
Family Nurse Practitioner, American Nurses Credentialing Corporation

ACADEMIC APPOINTMENTS

Assistant Professor, School of Medicine, University of Connecticut, 2006-present
Associate Professor, School of Nursing, University of Connecticut, Storrs, 2005-present.
Assistant Professor, School of Nursing**,** University of Connecticut, Storrs, 1999-2005.
Clinical Assistant Professor, School of Nursing, University of Massachusetts, Amherst, 1998-1999
Adjunct Assistant Professor, School of Nursing, University of Massachusetts, Amherst, 1995-1998
Clinical Instructor, School of Nursing, Yale University, 1985-1986
Clinical Preceptor, School of Nursing, University of Arizona, Tucson, 1985-1986
Clinical Preceptor, School of Nursing, University of Colorado, Denver, 1984-1986
Clinical Preceptor, College of Medicine and Dentistry, Newark, NJ, 1984-1985
Clinical Instructor, School of Medicine, Boston University, Boston, MA, 1983-1986

CLINICAL EXPERIENCE

Nurse Practitioner, Jewish Geriatric Services, Longmeadow, MA, 1991-1998
Nurse Midwife, OB-GYN Associates, Providence, RI, 1981-1983
Staff Nurse, Mary Breckinridge Hospital, Hyden, KY, 1978-1979
Staff Nurse, New York Hospital, NY, NY, 1977-1978

ADMINISTRATIVE EXPERIENCE

Nursing Supervisor, Jewish Nursing Home of Western MA, Longmeadow, 1990-1991
Director of Midwifery, Department of Health and Hospitals, Boston, MA, 1983-1986

AWARDS AND HONORS

Mary Lawrence Research Development Award, University of CT, 2004
Mary Lawrence Research Development Award, University of CT, 2001
American Nurses Foundation Scholar, 2000
Phi Kappa Phi Honor Society, 1997
Massachusetts Long Term Care Foundation Award, 1997
Joseph L. Boscov Fellowship, 1997
Traineeships for Doctoral Study, 1997-1999
Sigma Theta Tau Nursing Honor Society, 1977
Commonwealth Scholar, University of MA, 1971

FUNDING

Title	Agency	Type & #	Period	Total Direct Costs	Role
Mental and Physical Stressors in the Diagnosis of Breast Cancer: A multidisciplinary analysis of stress and systemic biomarkers in patients referred for biopsy of a suspected breast cancer lesion	The Connecticut Breast Health Initiative		2006-2007	$75,000	Co-Investigator
Translational Research in Breast Cancer Survivorship	University of Connecticut	Pauline A. Toner Fund	2006	$5,000	PI
Relationship of Neurocognitive Function to Breast Cancer Treatment and Induced Menopause	US Army Medical and Materiel Command, Breast Cancer Research Program	Clinical Nurse Research Award, W81XWH-04-1-0528	2004-2007	$199,997	PI
Research Training Program in Breast Cancer	US Army Medical and Materiel Command, Breast Cancer Research Program	DAMD 17-00-1-0509, Dr. Ruth McCorkle,PI	2002-2003	$38,712	Post-doctoral Fellow
Identification of Pain in Cognitively Impaired Elderly	American Nurses Foundation		2000-2002	$3,470	PI
Identification of Pain in Cognitively Impaired Elderly	Sigma Theta Tau		2000	$500	PI
Data Management for Pain and the Functional Status of Nursing Home Residents	University of Connecticut		2000	$1,000	PI

PUBLICATIONS

Kenefick, A.L. and McCorkle, R. (in preparation) Functional outcomes in older women after surgical treatment for breast cancer.

Kenefick, A.L., Swinney, J., and McCorkle, R. (in preparation). Racial disparity in symptom distress following breast cancer surgery.

Jones, B.A., Kenefick, A. L., Zinggeler, J. M., Dubrow, R., and Kasl, S.V. (under review). Delay, race, and breast cancer stage at diagnosis.

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Kenefick, A.L. and Schulman-Green D. (2004). Caring for cognitively impaired nursing home residents within. pain. *International Journal of Human Caring, 8*(2): 32-40.

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Kenefick, A. L. (1999). Low caloric intake predicted mortality for geriatric patients in hospital [commentary on (1998) Incalzi R. A., Capparella I., Gemma A. et al. Inadequate caloric intake: a risk factor for mortality of geriatric patients in the acute-care hospital. *Age Aging*, *27*(3), 303-10] *Evidence-Based Nursing*, *2*(1), 26.

Laufer, A. (1990). Breastfeeding: Toward resolution of the unsatisfying birth experience. *Journal of Nurse-Midwifery, 35*(1), 42-45.

Laufer, A. (1990). [Review of the book *VBAC sourcebook*]. *Journal of Nurse-Midwifery, 35*(1), 62.

Laufer, A. (1989). [Review of the book *The complete cervical cap guide*]. *Journal of Nurse-Midwifery, 34*(1), 52.

Laufer, A. (1988). [Review of the book *A flower garden: All about it, the diary of a woman's thoughts after cesarean birth]*. *Journal of Nurse-Midwifery*, *33*(5), 241.

Laufer A., Hodenius V., Friedman L., Duncan N., Guy C., MacPherson S., Barrows N. (1987). Vaginal birth after cesarean section: Nurse-midwifery management. *Journal of Nurse-Midwifery, 32*(1), 41-47.

Laufer, A. (1986). [Review of the book *Breastfeeding success for working mothers*]. *Journal of Nurse-Midwifery, 31*(6), 299.

SELECTED PRESENTATIONS

Functional Dependency of Older Women After Breast Cancer Surgery, 9th National Conference on Cancer Nursing Research, Hollywood California, February 10, 2007.

Neurocognitive Symptoms in Patients with Cancer. Yale School of Nursing, January 8, 2007.

Participatory Research in Breast Cancer Survivorship, The Carole and Ray Neag Comprehensive Cancer Program: Third Annual Research Retreat, Water's Edge Resort & Spa, Westbrook, CT, 11/27/2006

Cognitive Changes in Patients with Cancer, Yale University School of Nursing, April 4, 2006.

Quality of Life Assessment in Cancer Clinical Trials, The Carole and Ray Neag Comprehensive Cancer Program: Second Annual Research Retreat, Water's Edge Resort & Spa, Westbrook, CT, 11/5/2005

Researching Symptom Experience Following Surgical Treatment of Breast Cancer, University of Connecticut Health Center, 5/19/2005

Patterns of Symptom Distress in Elderly Women with Breast Cancer. Poster, Distinguished Scholars Day, University of Connecticut, 4/14/ 2005

Patterns of Symptom Distress in Elderly Women with Breast Cancer. Paper, 17th Annual Scientific Sessions of the Eastern Nursing Research Society, 4/8/ 2005

Relationship of Neurocognitive Function to Breast Cancer Treatment and Induced Menopause, Neag Comprehensive Cancer Program, University of Connecticut Health Center, 12/16/ 2004

Innovative Program of Research in Breast Cancer, University of Connecticut School of Nursing Advisory Board and UConn Foundation, 10/1/ 2004

Questioning the Information on Delay and Racial Disparities in Breast Cancer Survival, Paper, Association of Women's Health, Obstetric and Neonatal Nurses Annual Convention, "Challenging the Status Quo" , 6/29/ 2004

Blaming the Victim? Blaming the System? The Relationship of Delay to Stage of Disease at the Time of Breast Cancer Diagnosis, Poster, Scholars' Day, University of Connecticut, 4/22/ 2004

Delay and Racial Disparity in Stage at Diagnosis in Women with Breast Cancer, Paper, 16th Annual Scientific Sessions of the Eastern Nursing Research Society, 4/3/2004

Caring About the Nursing Home Residents with Pain—What Nurses Do, Paper, International Association for Human Caring, Boston MA, 5/22/2002

The Model of Sequential Trials—How Nursing Home Nurses Treat Symptoms, Poster, International Association for Human Caring, Boston MA, 5/22/2002

Making Decisions About the Nursing Home Resident with Pain, Paper, Hartford (CT) Hospital Research Utilization Conference, 10/2001

The Model of Sequential Trials—How Nursing Home Nurses Treat Pain, Poster, Annual Research Day, University of Connecticut, 5/7/2001

Making Decisions About the Nursing Home Resident with Pain, Paper, Sigma Theta Tau (Mu Chapter), Annual Research Day, Rocky Hill, CT, 4/26/2001

The Model of Sequential Trials—How Nursing Home Nurses Treat Pain, Poster, Eastern Nursing Research Society Annual Scientific Sessions, Atlantic City, NJ, , 4/1-3/2001

Pain Increases the Likelihood of Depression in Nursing Home Residents, Poster, Eastern Nursing Research Society Annual Scientific Sessions, Atlantic City, NJ, 4/1-3/2001

Making Decisions About the Nursing Home Resident with Pain, Paper, Eastern Nursing Research Society Annual Scientific Sessions, Atlantic City, NJ, 4/1-3/2001

Correlates of Depression in Nursing Home Residents—Implications for Prevention and Treatment, Paper, Sigma Theta Tau Nursing Honor Society, Beta Zeta Chapter, Northampton, MA, 3/8/2001

Correlates of Depression in Nursing Home Residents, Poster, Sigma Theta Tau Nursing Honor Society, Mu Chapter Induction, Storrs, CT, 12/3/2000

Correlates of Depression in Nursing Home Residents, Paper, Hartford (CT) Hospital Research Utilization Conference, 10/13/2000

Correlates of Depression in Nursing Home Residents, Poster, Second Annual Research Day, University of Connecticut School of Nursing, 5/8/2000

Pain and the Functional Status of Nursing Home Residents, Poster Presentation, Annual Meeting of the American Society Pain Management Nurses, Washington, DC, 4/16/1999

Alzheimer's Disease, Chronic Disease in Contemporary Literature, Paper, Sigma Theta Tau Research Day, University of Massachusetts School of Nursing, Amherst, 4/22/1998

TEACHING EXPERIENCE

Nursing 234, Clinical Science IV. Concepts from pharmacology, microbiology, pathophysiology, and nutrition as they relate to child bearing, child rearing families. 2001-2002

Nursing 236, Parent-Child Nursing. Functional health patterns and clinical decision-making related to the care of the child bearing, child rearing family. 2001-2002

Nursing 350, Nursing Science. Analysis of the current state of nursing science and the application of

knowledge from this science and other disciplines to advanced nursing practice from historical, contemporary and futuristic perspectives. 2001-present

Nursing 356, Nursing Theories and Patterns of Knowing. This survey course introduces the student to the art and science of nursing practice. It explores the historical, empirical, ethical, esthetical, and personal knowing aspects of nursing praxis. The legal, educational, regulatory, and financial world of nursing is examined. The major theorists influencing the development and advancement of the profession are explored. 2003-present

Nursing 358, Statistical Methods in Nursing. Quantitative procedures including descriptive and inferential statistics, non-parametric approaches to data, and parametric analysis through factorial analysis of variance. 2007-present

Nursing 383, Primary Care I. Health promotion/disease prevention and the assessment and management of selected acute and chronic health problems, including respiratory, cardiovascular, and endocrine systems. For nurse-practitioner students. 2001

Nursing 384, Advanced Health Assessment. Principles and techniques of advanced physical assessment for nurse practitioner students. 1999, 2000

Nursing 385, Primary Care II, Assessment and management of selected acute and chronic health problems, focusing on endocrine, gastrointestinal, integumentary and genitourinary systems, women's health and behavioral health. 2005

Nursing 389, Primary Care Practicum I. Focus is health promotion/disease prevention and the clinical diagnosis and management of individuals experiencing common acute and chronic health problems of respiratory, cardiovascular, and endocrine systems. The role of the nurse in primary care is examined. Includes a seminar and 12 clinical hours per week. 2001

Nursing 392, Practicum in Advanced Practice Gerontological Nursing I. Focus is on health promotion/disease prevention and the clinical management of older adults experiencing common acute and chronic health problems of the respiratory, cardiovascular, and endocrine systems. Common clinical problems of older adults will be examined. Includes a seminar and 12 clinical hours per week. 2000

SERVICE

University

School of Nursing Dean Search Committee, 2006-2007
American Cancer Society Institutional Grant Review Board UCONN Health Center, 2006-present
Intercampus Interdisciplinary Oncology Program Steering Committee, 2006-present
UCONN Health Center Breast Cancer Research Cooperative, 2005- present
Multicultural Diversity Faculty Trainer, Offices of Multicultural Affairs, and Diversity and Equity, University of Connecticut, 2004-2005

School

Promotion, Tenure and Reappointment Committee, 2005-2006
PhD Program Evaluation Committee, UCONN School of Nursing, 2005-2006
PhD Admission and Progression Committee, 2003, 2005-2006
Financial Oversight Committee, 2002-2003
Curriculum and Courses Committee, 2002-present
Merit Committee, 2001-2002
Faculty Recruitment and Selection Committee, 2000-2002
Master of Science Admissions Committee, 2000-2001

Professional

Reviewer, Western Journal of Nursing Research, 2007-present
Survivorship, Quality of Life & Rehabilitation Special Interest Group, Oncology Nursing Society, 2006-present
Research Advocacy Network, 2006-present

Connecticut Geriatric Education Consortium, 2005-present
Grant Reviewer, Alzheimer's Association, 2004-present
Advanced Nursing Research Special Interest Group, Oncology Nursing Society, 2002-2006
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Abstract Reviewer, Eastern Nursing Research Society, 2001-2003
Client Services Committee, Jewish Geriatric Services, Inc., Longmeadow, MA, 2001-2002
Grants Reviewer, American Society of Pain Management Nurses, 2000-2003
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Patterns of Symptom Distress in Older Women After Surgical Treatment for Breast Cancer

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Purpose/Objectives: To describe patterns of symptom distress over time in older women receiving surgical treatment for breast cancer and to examine the relationship of selected patient and clinical characteristics to symptom distress.

Design: Secondary analysis of breast cancer data from a prospective, longitudinal study of older patients with several types of cancer.

Setting: Large mid-Atlantic teaching hospital.

Sample: 57 patients with breast cancer participated. Subjects had a mean age of 68 and were predominantly white, not Hispanic, married, Protestant, retired, and in stage I or II. A total of 55 subjects completed the study.

Methods: The Symptom Distress Scale was used. Data were collected on discharge and at three and six months postdischarge. Descriptive statistics, t test, analysis of variance, correlation coefficients, and stepwise multiple regression were analyzed.

Main Research Variables: Total symptom distress and 13 individual symptom scores.

Findings: Fatigue, frequency of pain, outlook, and insomnia consistently were most prevalent and severe. Symptoms decreased gradually. Younger, more educated, and married women experienced more distress.

Conclusions: Interactions among symptoms are complex. Later symptom distress may be predicted by early experience and demographic characteristics.

Implications for Nursing: Clinicians should inquire about symptom distress at each encounter, expect multiple symptoms, and anticipate greater symptom distress in patients who are younger, more educated, or married or living with a partner. In women with more severe, earlier symptom distress, nurses should intervene promptly. Research should determine interrelationships of symptoms and how they might be affected by contextual variables, describe critical attributes of the nurse-patient interaction that might mitigate symptom distress, characterize the relationship of symptom intensity and distress, clarify the mechanism of the relationship between marital status and symptom distress, and identify the effect of symptoms, individually and collectively, on survival and quality of life.

Key Points . . .

- ➤ Most new cases of invasive breast cancer occur in older women who will be treated with surgery.
- ➤ Fatigue, frequency of pain, outlook, and insomnia were the most distressing postsurgical symptoms reported and were experienced by more than half of the women throughout six months.
- ➤ Although individuals have unique patterns of postsurgical symptom distress, women who are younger, better educated, or married may experience greater distress.
- ➤ Later symptom distress can be predicted from knowledge of earlier symptom distress.

Breast cancer, the leading cause of cancer deaths among women worldwide (World Health Organization, 2006), is the most commonly diagnosed invasive cancer among women in the United States (Jemal et al., 2005). Of the approximately 200,000 American women diagnosed with invasive breast cancer each year, about 78% are older than 50 years (Department of Defense, 2005). Most of the women who seek treatment for breast cancer will undergo surgery, either lumpectomy or mastectomy with or without axillary node dissection.

Women experience an array of symptoms throughout the course of their diagnosis, treatment, and recovery, such as insomnia, mood disturbances, fatigue, and difficulties with concentration (Carpenter et al., 2004; Cimprich, 1999; Nail & Winningham, 1995). Treatment-related fatigue, sleep disturbances, pain, hot flashes, nausea, and vomiting occur during and after breast cancer treatment (Bower et al., 2000; Graf & Geller, 2003). Following treatment, in addition to the previously listed symptoms, women report lymphedema and decreased arm mobility, sexual difficulties, problems with memory and attention, being unhappy with their appearance, and having hot flashes, aches and pains, and muscle stiffness (Ganz et al., 2004).

Symptom management is a core aspect of nursing practice. Understanding is necessary to plan and carry out effective interventions to relieve symptoms. Measurement, using reliable and valid instruments, allows nurses to learn about the frequency and intensity of symptoms, how the phenomena change over time, and their relationship to other variables.

The purpose of the current study was to describe the patterns of symptom distress over time in older women receiving surgical treatment for breast cancer and to examine the

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relationship of selected patient and clinical characteristics to symptom distress. Because breast cancer incidence and mortality increase with age (Lacey, Devesa, & Brinton, 2002), an understanding of the nature of the symptom experience of older women following initial surgical treatment for breast cancer is necessary to plan interventions that are appropriate, acceptable, and effective in mitigating symptom distress and improving quality of life. Such understanding will allow identification and remediation of the difficulties that older women have at home, potentially diminishing undesirable effects of burdensome symptom distress.

Related Literature

Symptoms

Symptoms are perceived indicators of change in healthy functioning as experienced by patients (Hegyvary, 1993). They are multidimensional, having subjective, perceptional, and experiential characteristics (Dodd, Janson, et al., 2001; Teel, Meek, McNamara, & Watson, 1997). These characteristics include both the physiologic sensations that signal patients that some internal condition is different and the interpretive processes that motivate patients to construct meanings for the symptoms and decide how to respond to them (Dabbs et al., 2004). Symptoms disrupt function, most notably social function and communication. Symptom outcomes include functional and emotional status, healthcare service use, mortality, morbidity, financial status, self-care, and self-management (Caldwell & Miaskowski, 2000; Dodd, Miaskowski, & Paul, 2001; Kenefick, 1999, 2004; Reishtein, 2005).

Symptom Distress

Symptom distress is the degree of perceived discomfort experienced in relation to a symptom (McCorkle & Young, 1978). Symptom distress affects the quality of life and survival of patients with cancer (Fu, LeMone, & McDaniel, 2004), and increased symptom distress has been associated with increased mortality (Degner & Sloan, 1995). The term *symptom distress* implies more than intensity. Symptom distress reflects symptom experience. The extent of symptom distress is determined by a person's sense of departure from healthy function, sensation, or experience in combination with the individual's interpretation of the importance of these events (McDaniel & Rhodes, 1995). The experience of multiple simultaneous symptoms has a synergistic effect on symptom distress (Lenz, Pugh, Milligan, Gift, & Suppe, 1997). Symptom distress is affected by and influences activities performed by patients or their advocates to relieve the symptom or prevent it from occurring. Symptom distress is an outcome indicator for symptom management.

Methods

Design

This article reports a secondary analysis of data from a larger study of the effect of a short-term nursing intervention on the quality of life of older patients newly diagnosed with several types of cancer (McCorkle et al., 2000). Secondary analysis contributes to knowledge development by allowing an opportunity for the researcher to examine previously collected data for a new purpose. Secondary analysis is an efficient and economic technique used to explore a particular subgroup of the original sample (Polit & Hungler, 1995). The current study's analysis focuses on the symptom distress of older women with breast cancer. The purpose of the present analysis is to describe the patterns of symptom distress over time in older women receiving surgical treatment for breast cancer and to examine the relationship of selected patient and clinical characteristics to symptom distress. In contrast, the purpose of the parent study was to examine the effect of home nursing care interventions on clinical and psychosocial outcomes among 375 participants with lung, breast, colorectal, head and neck, prostate, urologic, or gynecologic cancer. The parent study's design was longitudinal, with data collected from the same subjects on discharge from the hospital and three and six months postdischarge by the same researcher using standardized procedures and instruments. In this type of study, the same group of subjects supplies data at multiple points in time, allowing patterns of change to be revealed. This approach is useful to identify the effect of conditions and characteristics on health outcomes (Polit & Hungler).

Sample

The original study had 375 subjects aged 60–92 years who were newly diagnosed with solid cancers. The subjects were recruited from a large mid-Atlantic teaching hospital, and institutional review board approval and subject informed consent were obtained. Subjects for the study described in this article were those from the original study who had breast cancer. The patients had had definitive primary surgical treatment for breast cancer and a prognosis of greater than six months. They were 60 years of age or older and discharged from the hospital with a physician's order for follow-up care related to one or more high-technology, complex procedure or treatment.

Instrument

The outcome measure of interest in this study was symptom distress (i.e., the degree of discomfort from specific symptoms as reported by the patient). The **Symptom Distress Scale** (McCorkle & Young, 1983) is a reliable and valid measure of this outcome (McCorkle, Cooley, & Shea, 1998). The scale contains 13 cards, each representing a different symptom and including a five-point Likert-type scale of distress severity. Items used in the scale are appetite, insomnia, frequency of pain, severity of pain, fatigue, bowel pattern, concentration, appearance, breathing, outlook, cough, frequency of nausea, and severity of nausea. The items reflect symptoms described as follows. *Appetite* reflects a subject's enjoyment of food. *Insomnia* reflects the ability to initiate and maintain sleep. *Frequency of pain* ranges from almost never to almost constantly. *Severity of pain* ranges from very mild to almost unbearable. *Fatigue* reflects frequency and severity of tiredness or exhaustion. *Bowel pattern* reflects discomfort related to changes in the usual bowel pattern. *Concentration* ranges from the normal ability to concentrate to perceived inability to concentrate at all. *Appearance* ranges from basically unchanged to drastically changed and includes elements of concern related to appearance. *Breathing* ranges from usually breathing normally to almost always having severe difficulty. *Outlook* includes being fearful, worried, and scared. *Cough* ranges from seldom to frequent, persistent, and severe. *Frequency of nausea* ranges from seldom to continually, whereas *severity of nausea* ranges from mild to being as sick as possible. For each

item, the scale of distress severity ranges from 1 (normal or no distress) to 5 (extreme distress). Subjects respond by circling the number that corresponds to their experience for that day. A total symptom distress score is the unweighted sum of the 13 items, ranging from 13–65. In this article, data related to individual items are reported using the item names found in the Symptom Distress Scale.

Statistical Procedures

Data were analyzed using the SPSS® (SPSS Inc., Chicago, IL) statistical package. Patient-related and clinical data were summarized with descriptive statistics, including frequencies, means, and standard deviations. Analysis of variance and t tests were used to assess differences in mean symptom scores among groups of subjects defined by demographic or clinical characteristics. Paired t-test analysis was used to examine symptom distress over time. Correlation coefficients identified relationships between symptoms. Stepwise multiple regression analysis was used to identify predictors of symptom distress.

Results

Description of the Sample

The study began with 57 patients with breast cancer. Attrition was minimal, with the loss of one subject by the second data collection point and an additional subject by the third data collection point. The sample was predominantly white, not of Hispanic origin, married, Protestant, and retired and did not live alone. The average subject was 68 years old, had completed 13 years of education, and had an annual income of more than $35,000 per year. Most of the subjects had been diagnosed with stage I or II breast cancer and two comorbidities. On average, they spent nearly three days in the hospital for a surgical treatment and experienced two initial complications of treatment (see Table 1).

Table 1. Demographic Characteristics of the Sample

Variable	n	%
Race		
White, not Hispanic	35	61
Black	21	37
Asian	1	2
Martial status		
Never married	5	9
Married	30	53
Separated or divorced	5	9
Widowed	17	30
Religion		
Protestant	28	49
Catholic	17	30
Jewish	8	14
None	3	5
Other	1	2
Employment		
Full-time	12	21
Part-time	4	7
Unemployed	2	4
Disabled	3	5
Retired	29	51
Homemaker	7	12
Lives alone		
No	41	72
Yes	16	28
Income ($)		
Less than 35,000	28	49
More than 35,000	29	51
Stage of disease		
I or II	54	95
III or IV	3	5

N = 57

Note. Because of rounding, not all percentages total 100.

Symptom Distress Over Time

Mean total symptom distress scores were 23.81 (SD = 6.60) at discharge, 20.52 (SD = 5.04) at three months postdischarge, and 18.60 (SD = 4.50) at six months postdischarge. Scores remained near the upper limit of the range defined in the literature as "low" (i.e., 13–24) (McCorkle et al., 1998). The decrease in total symptom distress was statistically significant ($p < 0.01$) between each of the three measurement points. From discharge to three months postdischarge, the difference was 3.34 (SD = 7.11). From three to six months postdischarge, the mean change was less in amount and variability (1.98, SD = 4.63). The greatest mean change and greatest variability were noted when comparing the discharge scores to the six-month scores (5.45, SD = 7.30) (see Figure 1).

The mean number of symptoms per subject remained the same (six) at discharge and three months, dropping to four at six months postdischarge. At each of the three points, the most severe and frequently occurring symptoms were fatigue, frequency of pain, outlook, and insomnia, in that order (see Figure 2). Relative severity of the four symptoms remained constant over time. Absolute severity of the four symptoms diminished over time (see Figure 3); however, more than half of the sample continued to experience the symptoms throughout the study period. Fatigue distress diminished significantly (total mean difference = 0.40, $p < 0.04$) from discharge to six months postdischarge but not from discharge to three months postdischarge or from three to six months. Distress cause by pain frequency (total mean change = 0.49, $p < 0.05$) and outlook (total mean change = 0.60, $p < 0.01$) showed the same pattern. Distress caused by insomnia decreased significantly from discharge to three months postdischarge (mean difference = 0.39, $p < 0.05$) and from discharge to six months postdischarge (mean difference = 0.62, $p < 0.01$), but not appreciably from three to six months.

Correlations Among Symptoms

Pearson correlations with a p value of less than 0.05 were noted at all three times (see Table 2).

Appearance: Distress caused by appearance correlated with distress resulting from outlook at all three measurement points.

Appetite: Subjects with distress related to appetite were likely to experience a large number of other symptoms, including insomnia, nausea, fatigue, bowel pattern, and distress caused by concentration, appearance, and outlook.

Fatigue: Subjects with fatigue were likely to experience distress caused by bowel pattern, concentration, and outlook. Four of the six correlates of fatigue at three months were associated with the digestive system: appetite, bowel pattern, nausea frequency, and nausea severity.

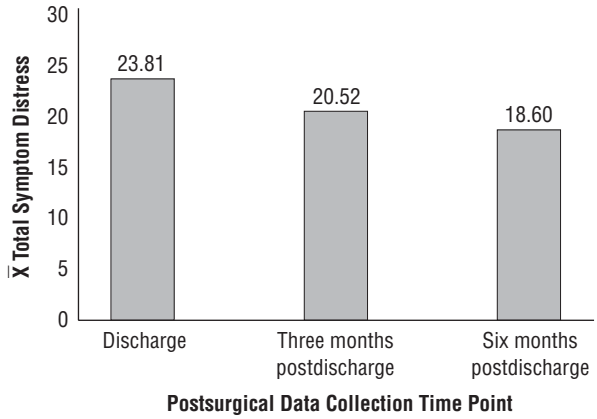

Figure 1. Mean Total Symptom Distress Over Time

Insomnia: Subjects with insomnia were likely to experience distress related to pain frequency and severity, fatigue, bowel pattern, concentration, appearance, breathing, and outlook. Individuals expressing distress related to insomnia by six months postdiagnosis were likely to have any of nine different symptoms.

Nausea: Significant correlations were found between severity and frequency of nausea at each of the three measurement points. Subjects with nausea were likely to experience distress related to appetite, insomnia, frequency of pain, fatigue, bowel pattern, breathing, and outlook.

Outlook: Outlook was associated with distress related to concentration and appearance at all three measurement points. Subjects distressed by their appearance on discharge from the hospital also expressed distress related to outlook. Distress related to outlook at six months was associated with distress caused by appearance, appetite, bowel pattern, concentration, insomnia, nausea frequency, and pain frequency.

Pain: Frequency and severity of pain correlated strongly with one another. Subjects with pain were likely to report distress related to fatigue, concentration, breathing, and outlook.

Persistent correlations: In addition to severity or frequency of pain and nausea, three sets of correlations persisted over the three measurement times: (a) concentration and fatigue, (b) concentration and outlook, and (c) appearance and outlook. The complexity of interactions among symptoms is not well described by the calculation of correlation coefficients.

Relationship of Selected Characteristics to Symptom Distress

Education correlated with total symptom distress at discharge ($r = 0.34$, $p < 0.01$), whereas age correlated negatively with total symptom distress at discharge ($r = -0.27$, $p < 0.05$). Thus, more education and younger age were associated with greater symptom distress at discharge.

Analysis of variance and t tests were used to assess differences in mean symptom scores among groups of subjects defined by demographic or clinical characteristics. The only significant findings concerned the analysis of data on marital status. To achieve adequate group size to allow analysis, groups were collapsed. Subjects who never married, were separated or divorced, or were widowed were combined into one group called "single" for purposes of analysis. Subjects who were married or living with a partner were combined into a group called "married" for the purpose of analysis. At six months postdischarge, married subjects showed a greater variability in symptom distress and significantly higher mean scores for total symptom distress ($p = 0.0001$), insomnia ($p = 0.0001$), frequency of pain ($p = 0.026$), fatigue ($p = 0.039$), bowel pattern ($p = 0.032$), and concentration ($p = 0.019$). No significant difference was found in total symptom distress among single and married subjects at discharge and three months postdischarge, but married subjects reported significantly more distress related to frequency of nausea ($p = 0.018$) and frequency of pain ($p = 0.018$) at three months postdischarge (see Table 3).

Predicting Variance in Symptom Distress

Stepwise multiple regression analysis revealed a statistically significant model for predicting total symptom distress at each of the three measurement points. Education predicted 11.5% ($p = 0.01$) of the variance in symptom distress at discharge. The symptom distress score at discharge predicted 8.1% ($p = 0.03$) of the variance in symptom distress at three months postdischarge, and the symptom distress score at three months predicted 29.5% ($p < 0.00$) of the variance in symptom distress at six months postdischarge (see Table 4).

Discussion

Symptom Prevalence and Intensity

At all three measurement points, fatigue, frequency of pain, outlook, and insomnia had the highest mean scores,

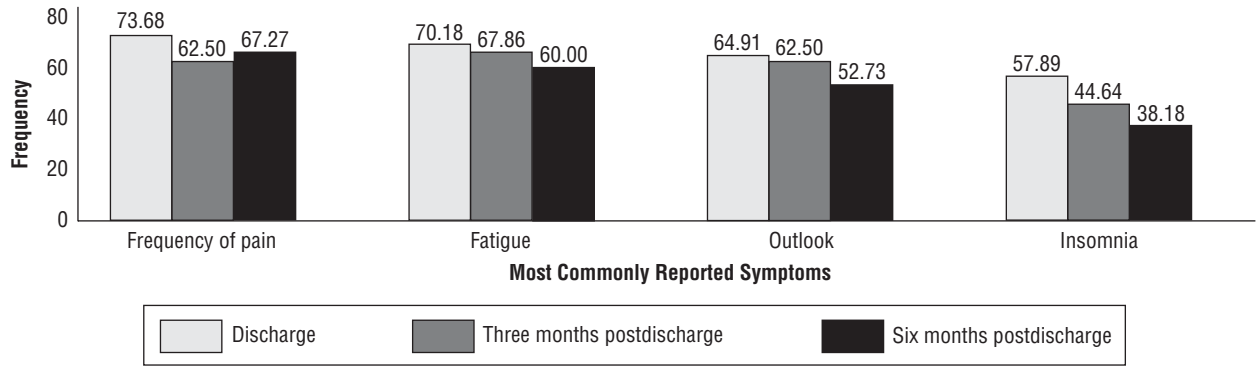

Figure 2. Frequency of the Most Commonly Reported Symptoms Over Time

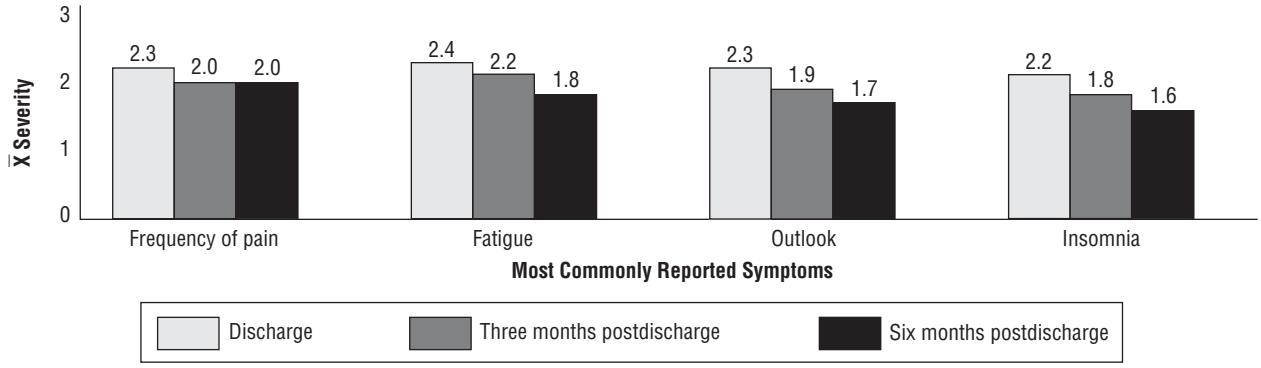

Figure 3. Mean Severity of the Most Commonly Reported Symptoms Over Time

representing primary sources of symptom distress. Pain and fatigue commonly are ranked as the most distressing symptoms by patients with cancer of other types (e.g., lung, breast, genitourinary system) (Cooley, Short, & Moriarty, 2003). These findings are similar to the lack of energy, worry, pain, and nausea reported by seriously ill patients with cancer (Tranmer et al., 2003). Findings have been similar in patients posthysterectomy who reported pain, sleep disturbances, depressed mood, and anxiety (Kim & Lee, 2001) and in patients with early-stage breast cancer who reported fatigue, appearance, insomnia, and concentration (Boehmke, 2004). Among patients with lung cancer, fatigue has been reported as the most frequent, intense, and limiting symptom (Gift, Jablonski, Stommel, & Given, 2004). Insomnia is a well-known problem among newly diagnosed or recently treated patients with cancer (Savard & Morin, 2001). In addition, pain is a common postoperative phenomenon.

Extent of Symptom Distress Over Time

Levels of symptom distress in the current study's sample generally were low and diminished over the six months of study data. Although the absolute intensity of distress related to fatigue, frequency of pain, insomnia, and outlook decreased over time, the symptoms continued to be experienced widely throughout the study period, each affecting half to two-thirds of the subjects at any time. However, the number of symptoms decreased during the period of the study.

The greatest decrease in total symptom distress occurred from hospital discharge to the three-month measure. Consistent with this research, other studies have shown that symptom distress levels in women with early-stage breast cancer generally are low. For example, a study of women prior to their first chemotherapy treatment showed a mean symptom distress score of 23 with a standard deviation of 4.2 (Boehmke, 2004). The present study of women following initial surgical treatment demonstrated a similar mean symptom distress score at the first measurement point (23.8) but showed greater variability at each of the three data collection points (standard deviations of 6.50, 5.04, and 4.50). Mean symptom distress scores at all three measurement points in this study (23.81, 20.52, 18.60) were higher than the pretreatment score ($\bar{X}$ = 18.10) reported for women older than 55 by Cimprich (1999).

Trends in Significant Correlations Among Symptoms Over Time

A number of significant correlations among symptoms were noted, suggesting a complex network of symptom experience. Similar to this study, other research has demonstrated correlations between severe fatigue and significantly higher levels of depression, pain, and sleep disturbance (Bower et al., 2000). The nature of the complex interactions among these symptoms remains unclear; however, the pattern of the interactions likely varies from one individual to another.

Influence of Patient or Clinical Characteristics

Age and education: The current study found that older subjects reported less total symptom distress at the initial measurement than did younger subjects. Other researchers also have found a negative correlation between age and symptom distress (Degner & Sloan, 1995), with a larger number of older patients reporting less symptom distress. Whether this is an issue of perception or appraisal is unclear. Decreased perception of pain has been noted among older patients with a variety of diagnoses, and research has demonstrated slowing of pain signal processing as well as decreased sensitivity to stimuli (Fass, Pulliam, Johnson, Garewal, & Sampliner, 2000; Moore & Clinch, 2004). Diagnosis of and treatment for breast cancer may have held different meaning and significance for the younger women in this study, contributing to greater expression of symptom distress when compared to the older women. Older women may have had more experience with the healthcare system and thus may have had more opportunities to develop mastery in dealing with healthcare situations. Expectations regarding the likelihood of receiving a diagnosis of cancer might be different in older woman, whereas the diagnosis may be perceived as more shocking or threatening to younger women. Additionally, the extent of surgery might vary with age (e.g., younger women experiencing more aggressive treatment).

The concepts of perception and appraisal may explain the increased severity of symptom distress among more educated women. As in the case of age, education may contribute to a different impression of the meaning and significance of the cancer experience, resulting in more expression of symptom distress.

Marital status and symptom distress: This study found a relationship between marital status and symptom distress

Table 2. Significant Correlations Among Symptoms Over Time

	Symptom Correlates at Three Intervals		
Symptom	**Discharge**	**Three Months Postdischarge**	**Six Months Postdischarge**
Appearance	Concentration, outlook	Appetite, concentration, outlook	Outlook
Appetite	Concentration, insomnia, nausea severity, outlook, pain frequency	Appearance, fatigue, insomnia, nausea frequency, nausea severity, pain frequency	Bowel pattern, concentration, outlook
Bowel pattern	Nausea frequency, nausea severity	Fatigue, nausea severity	Appetite, nausea frequency, outlook
Breathing	–	Pain severity, nausea severity	Insomnia, pain frequency
Concentration	Appearance, appetite, fatigue, insomnia, outlook	Fatigue, outlook	Appetite, outlook, pain frequency
Fatigue	Concentration, insomnia, outlook, pain frequency	Appetite, bowel pattern, concentration, nausea frequency, nausea severity, outlook	Concentration, nausea severity, pain frequency
Insomnia	Appetite, concentration, fatigue, outlook	Appetite, pain severity	Bowel pattern, concentration, fatigue, insomnia, nausea frequency, nausea severity, outlook, pain frequency, pain severity
Nausea frequency	Bowel pattern, nausea severity	Appetite, fatigue, nausea severity, pain frequency	Bowel pattern, insomnia, nausea severity, outlook
Nausea severity	Appetite, bowel pattern, nausea frequency, outlook	Appetite, bowel pattern, breathing, fatigue, nausea frequency	Insomnia, fatigue, nausea frequency
Outlook	Appearance, appetite, concentration, fatigue, insomnia, nausea severity	Concentration, fatigue	Appearance, appetite, bowel pattern, nausea frequency, pain frequency, concentration
Pain frequency	Appetite, fatigue, pain severity	Nausea frequency, pain severity	Concentration, fatigue, insomnia, outlook, pain severity
Pain severity	Pain frequency	Breathing, insomnia, pain frequency	Pain frequency

at three and six months postdischarge. Subjects who were married or living with partners reported more symptom distress than did the remainder of the subjects. The mechanism of this phenomenon is unclear. The presence or absence of significant interpersonal relationships affects the appraisal of life events. Research has demonstrated relationships between symptoms and psychosocial resources, gender, and perceived stress (Leidy, 1990). In addition, Tishelman, Taube, and Sachs (1991) suggested that reinforcement from supportive individuals legitimizes the experience of symptom distress, leading to increased expression of such distress. Sources of informational, tangible, and emotional support have been found to vary with marital status. Married women have identified their husbands as their most frequent providers of informational, tangible, and emotional support. Women who were widowed, divorced, or separated identified their children as their most common emotional support sources, other professionals as their most common informational support providers, and paid helpers as their most common tangible support sources (Friedman, 1993). Marital status might affect the perception of role demand, with the partner either sharing in tasks or requiring that the patient achieves a given level of role function despite surgery. The presence of a partner might affect the patient's own demands for role performance, and the presence of a marital relationship might alter characteristics of a woman's support system. The support system for married women might be restricted to their partner or to similar couples, whereas unmarried women might have a large support system composed of friends or they might be isolated from others. In this research, no relationship was found between symptom distress and whether subjects lived alone or with others.

Other patient and clinical characteristics: The current study did not demonstrate relationships between symptom distress and any other patient characteristics such as income, employment status, religion, or race. No relationships were identified between symptom distress at any time and clinical characteristics, including the number of comorbidities or initial complications and the length of hospitalization. The variance in the sample's data on stage of disease was insufficient to permit any conclusions about its relationship to symptoms.

Comorbidities have been recognized as complicating the treatment of cancer in older adults; however, weaknesses in the development of their conceptualization and measure-

Table 3. Relationship of Marital Status to Symptom Distress

Group Statistics	n	$\bar{X}$	SD	t	df	p	$\bar{X}$ Difference	Lower 95% Confidence Interval	Higher 95% Confidence Interval
Three months postdischarge									
Frequency of nausea									
• Single	26	1.12	0.326	–	–	–	–	–	–
• Married	30	1.50	0.777	–2.473	40.053	0.018	–0.38	–0.70	–0.07
Frequency of pain									
• Single	26	1.62	0.941	–	–	–	–	–	–
• Married	30	2.37	0.964	–2.945	53.210	0.005	–0.75	–1.26	–0.24
Six months postdischarge									
Insomnia									
• Single	25	1.16	0.624	–	–	–	–	–	–
• Married	30	2.03	1.098	–3.697	47.275	0.001	–0.87	–1.35	–0.40
Frequency of pain									
• Single	25	1.56	0.651	–	–	–	–	–	–
• Married	30	2.07	0.980	–2.290	50.659	0.026	–0.51	–0.95	–0.06
Fatigue									
• Single	25	1.72	0.980	–	–	–	–	–	–
• Married	30	2.23	0.774	–2.125	45.306	0.039	–0.51	–1.00	–0.03
Bowel pattern									
• Single	25	1.04	0.200	–	–	–	–	–	–
• Married	30	1.40	0.855	–2.234	32.763	0.032	–0.36	–0.69	–0.03
Concentration									
• Single	25	1.16	0.374	–	–	–	–	–	–
• Married	30	1.57	0.817	–2.436	42.199	0.019	–0.41	–0.74	–0.07
Total symptom distress									
• Single	25	16.60	2.990	–	–	–	–	–	–
• Married	30	20.27	4.890	–3.413	48.917	0.001	–3.67	–5.83	–1.51

ment limit their applicability to research and clinical practice (Satariano & Silliman, 2003). Comorbidity has been related to prognosis (Given, Given, Azzouz, & Stommel, 2001; Satariano & Silliman), but its relationship to symptom experience remains unclear. The number of symptoms, although associated with advanced disease, is thought to affect patient outcomes, including morbidity (Dodd, Miaskowski, et al., 2001). Among older patients with lung cancer, the number of comorbidities has been correlated with symptom severity (Kurtz, Kurtz, Stommel, Given, & Given, 1999). Symptom severity in this setting, in turn, has been correlated with a loss of physical functioning, which is a healthcare outcome (Kurtz et al., 2000).

Predicting symptom distress: Stepwise multiple regression analysis was used to identify variables that predicted significant variance in total symptom distress measures at any point in time. Education accounted for a small but statistically significant amount of the variance in symptom distress at discharge. At three months postdischarge, the only significant predictor was the score for symptom distress at time 1. Likewise, at six months postdischarge, the significant predictor was the previous measure, total symptom distress at time 2. The predictive value of the three-month score for the six-month score was greater in magnitude and significance than the other predictors.

Table 4. Predictors of Total Symptom Distress Score (SDS) at Three Points in Time

Time Period and Predictor	R^2	β	F	p
Discharge				
Education	0.115	0.339	7.165	0.01
Three months postdischarge				
SDS at discharge	0.081	0.284	4.730	0.03
Six months postdischarge				
SDS at three months postdischarge	0.295	0.543	21.750	0.00

Conclusions

Symptom distress declined slowly in the six months following breast cancer surgery. The rate of change was greater from discharge to three months postdischarge than from three to six months postdischarge. Fatigue, frequency of pain, outlook, and insomnia remained primary sources of symptom distress throughout the six months of observation, independent of the length of time since surgery. In this study, younger women and those who were more highly educated experienced more symptom distress early in the postoperative period. Relative rankings for the type of symptom distress remained the same over time. Subjects who reported more symptom distress early in their postoperative course continued to report more symptom distress throughout the six months, whereas those who reported less early symptom distress continued to report less symptom distress throughout the six months. Subjects who were married or living with a partner reported greater distress from selected symptoms at three months and greater total symptom distress at six months postdischarge. Interactions among symptoms are complex and are not well modeled with statistical analysis.

This research is limited because it did not consider the possible effects of postoperative chemotherapy, biotherapy, radiation, or hormone therapy given during the period of the study; however, the study does describe the symptom experience of a group of older women following surgery. This population-based study sheds light on the nursing care needs of a population defined by age rather than by use of adjunct therapies. The current study's research has clinical implications for practicing nurses and theoretical implications for researchers.

Recommendations for Clinical Applications

When caring for older women having breast cancer surgery, nurses should inquire about symptom distress at each encounter and provide appropriate anticipatory guidance. Nurses should expect to find distress related to fatigue, frequency of pain, outlook, and insomnia but appreciate the individuality of the symptom distress experience. The use of a standardized instrument, such as the Symptom Distress Scale, should be accompanied by discussion with the patient. However, nurses should note that allowing or encouraging the expression of symptom distress could result in increased expression of such distress. The increased expression could be incorrectly assumed to reflect an increase in perceived symptom distress when compared to women who are less expressive. In other words, nurses cannot always assume that women who express their distress experience more distress and, conversely, women who do not express distress do not experience distress.

Because breast cancer is so prevalent, patients often are compared to others with the disease. Nurses should look for higher levels of distress in married women, particularly at three months postdischarge. Nurses should anticipate greater symptom distress in patients who are younger and more educated and in those with more severe, earlier symptom distress. Symptoms rarely occur in isolation, and their interactions are complex. Patients with one symptom are likely to have others as well. Patients should be asked about other symptoms and their impression of how the symptoms might be related. Because the greatest change in symptom distress occurs during the first three months after discharge, little change during this period of time is a matter of concern. Nurses should act to minimize symptom distress earlier to minimize it later.

Total symptom distress may be reduced substantially by a well-targeted intervention that decreases distress caused by several symptoms. Topics of interest for clinicians include methods of treating more than one symptom at a time and strategies for establishing symptom treatment priorities. Approaches in which nurses can leverage the side effects of a primary symptom treatment to diminish other symptoms are important to identify. Nurses should consider treatment options for one symptom that may result in the improvement of another symptom. For example, the side effects of one treatment may be seen as therapeutic for another symptom, such as when an analgesic medication that has a side effect of drowsiness is given at bedtime to a patient with pain and insomnia. The patient may experience pain relief while being able to fall asleep easier.

Research Implications

Researchers should study the natural history over time of symptoms relative to each other, clarifying relationships such as interaction and causation. Researchers should seek to identify contextual variables that affect the magnitude of symptoms, individually and in combination, identifying the phenomena that can be manipulated therapeutically to diminish symptom distress. To clarify the role of social support in adaptive responses to illness, the mechanisms of the relationship between marital status and symptom distress should be identified clearly.

Another topic of interest to researchers is the relationship of symptom distress to symptom intensity and the critical attributes of the nurse-patient interaction that mitigate symptom distress. A novel way of understanding patient characteristics might include determination of an individual symptom distress style (i.e., the way a person has exhibited symptom distress in the past and presumably will do so in the future). An individual's personal symptom distress style would be defined by the conditions under which distress has occurred, how it was perceived and expressed, its extent and duration, what relieved it, what exacerbated it, and its effect on the person's functional status. If research establishes that individuals have unique personal symptom distress styles, knowledge of a person's history of symptom distress might be useful in anticipating the experience in a new situation and in planning care.

This article contributes to the body of literature describing patients' experiences with symptoms associated with cancer treatment. The findings suggest a need for strategies based on understanding of the relationship between patient characteristics and symptom distress. Additional work is needed to understand the effect of symptoms, individually and in combination, on patients' survival and quality of life.

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Decision Making in Pain Management Using the Model of Sequential Trials

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This article describes the use of nursing art to solve problems related to the management of pain in cognitively impaired persons who live in nursing homes. The result of naturalistic inquiry, the Model of Sequential Trials arose from a qualitative study of the beliefs, experiences, and behaviors of nurses managing pain in this context. The model illustrates a strategic process of evaluation, trials, reevaluation, and repeated trials that demonstrates the rationale and process underlying nursing management of pain. Future research is needed to evaluate the model's usefulness in other practice settings and in teaching clinical decision making.

Key words: *clinical decision making, cognitive impairment, nursing art, pain*

The purpose of this article is to present the Model of Sequential Trials (MOST). This model describes the process by which nurses make decisions regarding individualized pain management in cognitively impaired persons who live in nursing homes. The result of naturalistic inquiry, the model arose from a larger qualitative study. The purpose of the larger study was to describe the beliefs and behaviors of nurses as they managed pain in nursing home residents.

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In this article, we will first describe the context of pain management in nursing homes and the research methods that were used. Findings leading to the development of the model will be presented. The model will be described in detail and its significance discussed. Limitations and recommendations will follow.

THE CONTEXT OF PAIN MANAGEMENT IN NURSING HOMES

It has been well established that there is a high prevalence of pain among nursing home residents.[1] It has also been well documented that untreated pain is associated with deterioration in a variety of quality-of-life measurements, and that there are particular difficulties in management of pain in the nursing home setting.[2]

Previous studies have identified specific issues. For example, a common issue is that pain medications may be withheld if nurses are not sure that residents are experiencing pain at the time medications are to be given. Both medications that are scheduled to be given at regular intervals and those that are to be given as the nurse believes them to be necessary (prn) may be withheld. In some settings, however, pain medication may be given in anticipation of pain, not on the basis of the nurse's conclusion that the resident is actually in pain at the moment.[3]

Another issue arises from the poorly defined relationship between nurses' assessments and their response to the patient. Research has shown a lack of significant correlation between registered nurses' ratings of pain among the nursing home residents and the administration of pain medications.[4] A third issue is that psychotropic drugs are often used inappropriately to treat behaviors that may be caused by pain,[5] resulting in a patient's impaired ability to communicate, interact socially, and perform activities of daily living. Inappropriate use of psychotropic drugs can cause additional difficulties in pain management in this setting. Research has shown that despite the presence of painful conditions, more disoriented, withdrawn, and functionally impaired residents are administered significantly less pain medication by nursing staff,[6] leaving these residents at risk for uncontrolled pain.

Pain management in the nursing home is further complicated by the high prevalence of cognitive impairment in this population.[7–9] Cognitively impaired residents are prescribed significantly less scheduled medication and receive significantly less pain medication compared with the cognitively intact elderly.[4] While research has shown that nurses believe that cognitively impaired persons who live in nursing homes are no less likely to experience pain compared with nursing home residents who are cognitively intact, nurses are less likely to administer pain medications to those with cognitive impairment. For example, in a study of hip fracture patients, those who were cognitively impaired were found to score significantly higher on the Checklist of Nonverbal Pain Indicators, yet they received significantly less opioid analgesics compared with the cognitively intact subjects.[10]

The rationale and process of nursing management of pain in cognitively impaired persons who live in nursing homes is unclear. Given the specific issues as discussed above, it is important to understand the dynamics between the nurse and the cognitively impaired nursing home resident in specific situations. Several different models of situational problem solving have been proposed, but the relevance of these models to nursing practice has not been established. This study seeks to fill this gap by presenting a model of situational problem solving that is highly relevant to nursing practice.

RESEARCH METHODS

The study included semi-structured interviews, review of documentation, and participant observation of nursing care in a 200-bed suburban nursing home in southern New England. The nursing home was selected because the administration was supportive of nursing research, and therefore allowed easy access to the setting. Entrée was provided because the nurse-researcher had worked with these nurses in a collegial manner for several years. Trust had been developed and a sound professional relationship existed between the parties.

Participants

Semi-structured interviews were conducted with 3 key informants, all of whom were head nurses in the nursing home. The perspective of head nurses in the nursing home is of critical importance to the understanding of how nursing staff makes decisions because head nurses influence policy, evaluate practice, and serve as examples of expertise. Semi-structured interviews are useful in the investigation of complex issues such as clinical decision making. In this case, the researcher, knowing the informants, had the advantage of "already knowing the cast of characters."[11] Threats to validity of the data were minimized because the researcher was able to evaluate the respondent's nonverbal behaviors and to ensure that respondents were unable to receive input from anyone else while they were answering a question. The informants in this study were

selected because most residents in their 40-bed units had significant cognitive impairment. The informants were all women and all graduates of 2-year associate degree educational programs in local community colleges. Their ages were 25, 38, and 46 years. Years of experience in nursing were 3, 18, and 25. Before becoming a nurse, the youngest informant had worked for 3 years as a nursing assistant in the same nursing home.

Procedures

Individual, private, semi-structured interviews were conducted with each of the respondents. Interviews lasted from 45 to 60 minutes and were conducted in a private office at the nursing home. They were tape-recorded with the informed consent of the nurses. Nursing home residents were not identified in either the interviews or the transcriptions. During the interviews, nurses were asked to recall incidents from their practice and to discuss mock clinical scenarios. Data obtained from earlier parts of the interview were used to inform subsequent questions. For example, nurses were asked to relate a current topic (such as, difficulties in identifying pain) to the previous discussion of a resident with persistent agitation.

Analytic technique

A tape recorder was used to record interviews. Field notes were also kept. Journaling was used to record insights during the research process. The recorded interviews were transcribed and analyzed by the nurse-researcher. Narrative analysis was used to identify common themes or patterns that might describe nurses' experiences with pain in the cognitively impaired nursing home resident. Pertinent concepts were noted and theoretical linkages proposed. The model is a graphic representation of these findings.

FINDINGS LEADING TO THE DEVELOPMENT OF THE MODEL

As noted, the MOST was created on the basis of themes identified from interviews with key informants. Nurses described a process of pain management decision making that was based on symptom management and had 3 phases. They described developing a hypothesis regarding the resident's possible pain behavior, choosing a suitable pain therapy, and identifying a target pain behavior (TPB) with which to track the resident's response to pain therapy.

Developing the hypothesis

When asked to provide an example of clinical decision making, nurses talked about their approach to symptom management, particularly their experience with identification of pain behavior. For example, one nurse recalled having observed a cognitively impaired nursing home resident crying and limping. She reviewed the resident's history and noted a diagnosis of arthritis of the hip. She hypothesized that the resident was crying and limping as a result of a painful, arthritic hip. She administered a mild analgesic and observed for a change in the crying and limping. After an interval, she noted that the resident was no longer crying and was walking without a limp. She concluded that the resident's behavior was a result of the pain that he was experiencing because of his arthritic hip. She decided to ask for medical permission to start giving the mild analgesic every morning with the goal of promoting the resident's comfort while preventing impaired ambulation secondary to pain.

Selecting pain therapy based on a hypothesis

Nurses described the importance of forming a hypothesis and testing appropriate interventions in order to develop a response to the behaviorally expressed needs of the nursing home resident. Nurses believed that the underlying etiology of the problem might not be readily apparent. While treatment decisions were influenced by the nurse's previous experience with the resident, the decision-making process was increasingly difficult and complex when the resident was verbally or cognitively impaired. The process of selecting pain therapy was influenced by how well a nurse knew the resident. It became increasingly difficult and complex when the resident was verbally impaired. In these cases, knowledge of the person was particularly important. One nurse stated,

> You need to know the patient.

Another said,

> Maybe someone who is not verbal or is verbal and their cognitive functions are limited... and you know that in the past when you've administered a pain medication to this person it's knocked them out and you're unable to wake them for care or meals and it's now time for a meal and this resident is having pain... hard to decide. Do you let them have the meal first and give them something less effective for the pain, or do you give them what you think they need and let them sleep through a meal?

Identification of TPBs

Nurses described *TPBs* as nonverbal pain indicators, such as moaning, grimacing, or crying. Nurses noted that TPBs could also be functional difficulties such as limping, not eating, or the new onset of urinary incontinence.

A nurse reported,

> A resident might all of a sudden become incontinent or unable to dress herself and it might be because of pain. You have to consider that.

As pain therapy was underway, its success was evaluated by considering whether there had been any improvement in the TPB. Nurses viewed a decrease in the extent, severity, or frequency of the TPB as improvement and the pain therapy was continued. If the TPB did not improve, a new strategy was designed. Another nurse astutely summarized the process as follows:

> A lot of it is trial and error.

While the nurses expressed that adequate treatment of pain was an important part of their job, they also wanted to delay giving medications for as long as possible by trying other strategies first. Nurses reported that they preferred to administer analgesics only after unsuccessful trials of other pain-relieving modalities, such as distraction, activity, and massage.

> I would try and change their position maybe to not have so much weight bearing on that part of their body... get their attention off their pain and on to something else, bring them into an activity or bring them in front of a television... and if that still didn't work, then I would realize that the resident was really in pain and required something to relieve it.

> You have to make sure that you do everything you can do prior to administering the pain med. Once those are done then you give the medication.

Judging success or failure of a trial

The nurse would evaluate the frequency and intensity of the designated TPB. If the extent, severity, or frequency of the TPB diminished with treatment, the trial was considered successful. The success of a trial of an analgesic confirmed the nurse's assessment that the resident's behavior was indeed due to pain that was not easy to identify because of difficulties in communication. A nurse said,

> If the person can't express that they're in pain, they may act out in an agitated manner. Sometimes just a trial with a little bit of (a mild analgesic) to see if that helps calm the agitation.

A nurse explained,

> If she's less incontinent when she gets (acetaminophen) then you know she was really in pain all along and that was why she was incontinent.

When a trial was successful, nurses believed that the logic that had led to the intervention had been validated. Trials were judged successful because the TPB diminished in response to the nurse's intervention. For example, a nurse recalled,

> ...It worked... she stopped yelling.

Nurses believed that a trial was unsuccessful because of the logical or practical errors. This nurse described anticipating a new trial involving a change in modality.

> She continues to yell... So we'll give it another day or so, maybe increase the dosage, see if that works and if not, then go more toward the antianxiety med.

Other dynamics that affect pain management

Experience

None of the nurses described a formal routine for making decisions about the nursing home resident with pain. Nurses felt that their experience and time in practice enabled them to recognize and understand changes in the resident's condition without needing to go through the formalized process of data collection and analysis that was part of their jobs. They stated that it was the nurse's experience that allowed her to identify the resident's issues in general and pain in particular. For example, nurses said,

> Sometimes you just know.

> I've been doing it so long I can recognize problems in people without having to go through this (regulated assessment process) thing to pinpoint the problem. I know what the problem is.

Limited autonomy

Another dynamics affecting pain management was that in the nursing home, nurses have little autonomy relative to diagnostic reasoning. For example, one nurse said,

> If we feel... maybe... a urinary tract infection... you have to bring it to (the doctor's or the

nurse-practitioner's) attention so that the proper data can be collected.

Residents' characteristics

Because cognitive impairment influences the resident's interpretation of, and response to, sensory stimuli, nurses believed that cognitive impairment could affect the resident's ability to perceive, respond to, and communicate pain. While the nurses believed that cognitively impaired persons made perceptual and judgmental errors regarding sensory stimuli, they believed that the problem was not if the resident perceived pain. They believed that the problem was with the resident's ability to appropriately respond to the pain and communicate it to others. For example, a nurse said,

> These people may be suffering pain and they just can't tell us. Therefore, they're exhibiting it in other ways.

While knowledge of the resident's baseline was important, nurses stressed that they needed to remain open-minded, considering situational phenomena and differentiating something situational from "something really going on." Physical evidence was important in making this distinction.

> It's very important to know what their baseline is and what they're used to and to take almost everything else into consideration because it could be something in their shoe. It could be they had been sitting too long and just having a hard time getting started. It could be something actually going on and your assessment would be to find... some physical evidence that there was some inflammation or whatever is going on, and I think you have to really get really down to basics and find tactics to find out what's going on....

THE MODEL OF SEQUENTIAL TRIALS

The process that nurses used to treat pain in cognitively impaired persons who live in nursing homes is illustrated in Figure 1. The MOST depicts a branched tree of events and data that describes the process of decision making for patients in pain. It includes identifying a TPB of interest, selecting management strategy based on a hypothesis, and conducting a trial. Decisions are pragmatic, based on the nurse's own best judgment, and subject to repeated trials until the desired outcome is achieved. Each component of the model will be described in detail with clinical examples included.

Identify TPB

A trial begins with the nurse's determination of an individualized TPB. The TPB is specific to a given nursing home resident at the specific time and place of the interaction with the nurse. The TPB must be amenable to measurement, an observable phenomenon that correlates with the frequency and/or intensity of pain.

Select pain therapy based on a hypothesis

The nurse hypothesizes that the TPB is the result of a painful phenomenon. The nurse then selects a pain therapy based on the hypothetical pain stimulus-response pattern. The treatment addresses either the underlying cause of the pain or the pain itself. Treatments can include medications, behavioral interventions, complementary therapies, etc.

Conduct trial of pain management

A trial of the pain therapy is conducted. For example, if the nurse hypothesizes that the resident is limping because of ill-fitting shoes, a pain therapy could be the removal of the shoes with more suitable footwear substituted. In this example, the nurse addresses a possible underlying cause of the pain, selects an intervention, substitutes footwear, and prepares to observe for a change in the limping behavior.

Evaluate frequency and intensity of TPB

Success or failure of a trial is determined by the nurse's evaluation of changes in the frequency and intensity of the TPB. A decrease in frequency or intensity of the target behavior implies that the pain therapy has been effective in relieving the pain and the therapy can be continued. As seen in the model, if the resident's TPB has improved, the nurse will continue the treatment. At some point, the TPB will be so diminished that the nurse will reevaluate the necessity of continuing treatment and may stop the treatment if it is not needed any longer.

Insufficient decrease, lack of change, or an increase in frequency or intensity of the pain behavior implies that an error has occurred. Errors may be of 2 types: diagnostic error and treatment error. Discussion of a typology of errors is presented below.

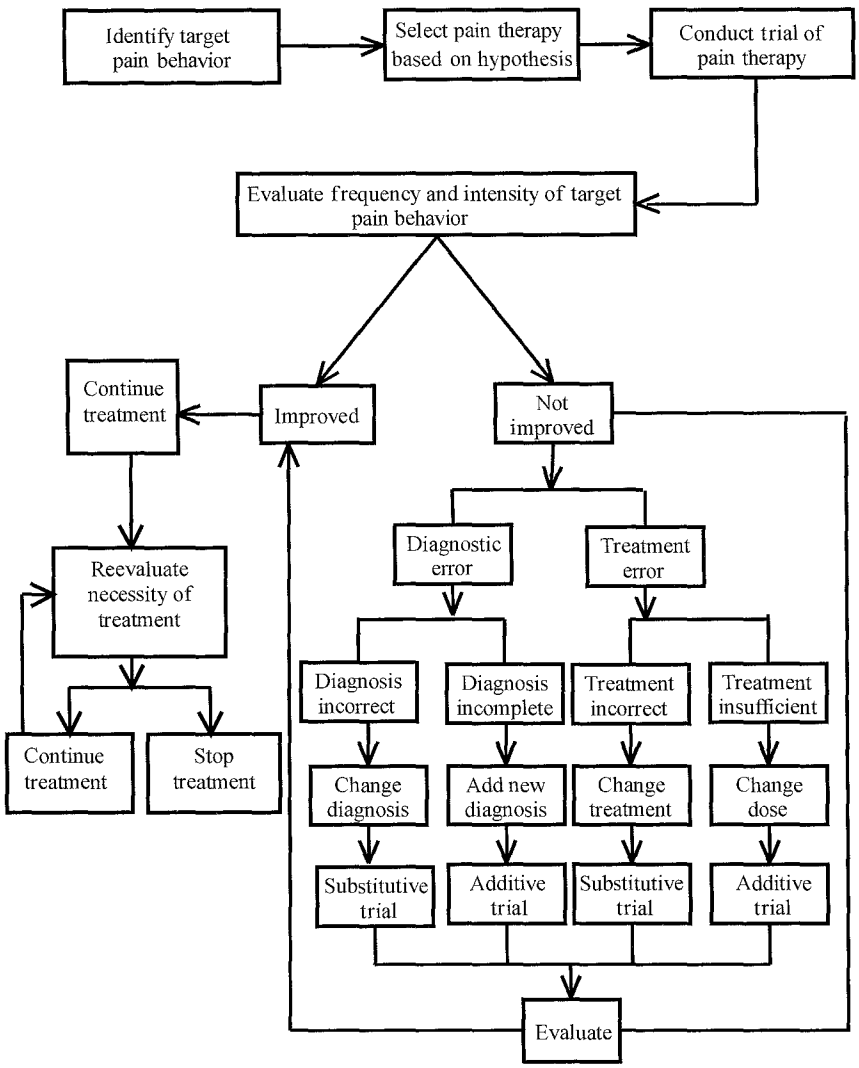

Figure 1. Model of Sequential Trials.

Diagnostic errors

Diagnostic errors are related to the nurse's hypothesis about the underlying cause of resident's behavior. Diagnostic errors are of 2 types: (1) diagnosis, incorrect and (2) diagnosis, incomplete. For example, consider the example of a resident, with a history of arthritis of the hip, who is limping and crying. The nurse hypothesizes that the resident has pain due to the arthritis and administers an oral analgesic. If the resident does not show an improvement in the TPB of limping and crying after being treated with an oral analgesic, it might be that the resident has pain because he is wearing uncomfortable, ill-fitting shoes that belonged to another resident. In this case, the resident's medical diagnosis of hip arthritis is not significantly contributing to his TPB. This would indicate an incorrect diagnosis. If the resident's arthritis were active and he were wearing someone else's shoes, as well, this would be an example of an incomplete diagnosis. In each case, as long as the resident continued to wear the wrong shoes, he would have an unaddressed cause of pain and difficulty walking. Another example of an incomplete diagnosis would be if the resident were indeed limping from his arthritis but crying due to sadness about something else.

Treatment errors

Treatment errors may be classified similarly. Treatment errors are also of 2 types: (1) treatment incorrect, and

(2) treatment insufficient. An incorrect treatment of the resident in the previous example might have been changing the ill-fitting shoes when the pain was actually due to fecal impaction. A commonly occurring example of insufficient treatment is administering a subtherapeutic dose of a medication. For example, 81 mg of aspirin, while useful for its anticoagulant properties, is not an effective dose for pain relief. The choice of responses to the problem of insufficient treatment includes (1) increasing the dose of a medication, (2) adding another medication, or (3) both increasing a dose and adding another medication. For example, the nursing home resident with unrelieved chronic pain may be offered an adjuvant analgesic, such as an anti-inflammatory drug. This can occur with or without an increase in the dose or frequency of other analgesics that the resident was already using.

Types of new trials

The typology of trials is related to typology of errors and is discussed below. Changing treatment hypotheses or diagnostic hypotheses results in the design and implementation of new therapeutic trials. These trials may be described as additive or substitutive. Both additive and substitutive new trials could result from the nurse considering alternative hypotheses that might explain the resident's behavior. The designation is based on characterizing the new treatment in comparison to the treatment in the unsuccessful trial.

In *substitutive trials*, the preceding treatment is abandoned and replaced by a new treatment. For example, a mild analgesic does not appear to be helpful in reducing behavioral evidence of pain, so it is discontinued, and a different, more powerful analgesic is given instead. Alternatively, a complementary therapy, such as massage, could be used.

A new additive trial could result from the nurse's suspicion that the dose of an analgesic was insufficient. *Additive trials* may include increasing the dose of a drug or adding a new drug to be given in addition to the original drug. Additive trials have 2 forms. These are the dose-related additive trial and the modal additive trial. In the former trial, the intensity of the treatment is changed. This may include changing the dosage, frequency, and/or duration of treatment. The expression "dosage" typically refers to medications. It includes increasing or decreasing the number of units of measure, for example, milligrams. Changing the number of doses may occur with or without changing the total dosage per day. To change the number of doses without changing the total amount of medication, the amount of medication per dose is adjusted.

The concept of dose is related to the concepts of frequency and duration. Both frequency and duration are applicable to treatments such as compresses, baths, massages, and music therapy. These treatments are commonly ordered to be carried out for a specified period, for example, "warm soaks for 20 minutes." In the *modal additive trial*, the original treatment is retained and a new treatment is added to the plan. For example, the nurse might decide to begin application of warm compresses while continuing to administer a mild analgesic.

While substitutive and additive trials may be carried out concurrently, doing so may be unsatisfying to the nurse who is using the resident's response to treatment as a means of understanding the resident's behavior. Trials are evaluated in terms of how much they changed the TPB, that is, how much they ameliorated the resident's apparent distress. If the TPB does not change significantly for the better, the question of diagnostic and therapeutic errors is revisited. The nurse seeks evidence of incorrect/incomplete diagnoses or incorrect/insufficient treatment. New trials are devised and implemented on the basis of these findings, and the cycle of sequential trials continues.

DISCUSSION

The proposed model describes the nursing management of pain in situations where the resident has cognitive impairment. It demonstrates that the use of behavioral evidence of pain can be valuable in planning nursing care when verbal communication is inadequate. It contributes to understanding patterns of interaction between nurses and those for whom they care. This article presents the MOST in detail and describes how it arose. Because the MOST arose from the analysis of the clinical practice of nursing, it has several potential applications to the study of the clinical practice of nursing. First, the model could allow evaluation of nursing behavior and be used to facilitate improvement in practice. Second, it could allow identification of errors in logic that occur during the process of assessment and management, and facilitate adjustment in thinking.

While the graphic representation of the MOST resembles other branched structures, it is distinct from a decision tree or algorithm because it is descriptive, not prescriptive. The MOST illustrates the rationale and process underlying nursing management of pain in cognitively impaired persons who live in nursing homes. It reflects nursing's practical concern with finding the correct

relationship between means and ends.[12] It illustrates how nursing knowledge of both the individual resident and the geriatric nursing is used to develop and revise a plan of nursing care useful to relieve an individual's pain in a particular time and place. That success is defined as achieving the desired outcome (a decrease in pain behavior) and is characteristic of the practical knowledge.[12] The MOST includes both the retrospective, reflective, and evaluative aspects of critical thinking and the generative quality of creative thinking.[13]

The MOST represents a strategic process of evaluation, trials, reevaluation, and repeated trials. Nurses used their knowledge of individual residents as a means of understanding the resident's behavior that might represent pain. They identified the resident's TPBs, hypothesized about the cause of the behavior, and developed treatment strategies designed to address their hypotheses.

This article describes the use of art of nursing to solve problems related to the management of pain in cognitively impaired persons who live in nursing homes. Determining an appropriate course of action in response to a unique clinical situation is a major component of the art of nursing.[14] The MOST is a model of nursing that begins with the nurse's identification of the individualized pain-related behavior. The nurse identifies a nursing home resident's unitary, evolving pattern, describing the meaning of the resident's behavior in context, over time, consistent with the conceptualization of a nursing praxis based on pattern recognition.[15]

Models for diagnostic reasoning

The diagnostic reasoning in which physicians typically engage in a clinical setting is *theoretical reasoning*—a search for the truth. By contrast, what nurses typically do in a clinical setting is *practical reasoning*—a search for an action plan. Analysis of clinical decision making in the context of nursing practice[16] reveals a process of making specific individual choices based on rationales that might be categorized as either "medical" or "nursing" knowledge. Nurses often use models of intuition and pattern recognition.[17] Whether using practical or theoretical reasoning, choices are based on the nurses' assessment of the individual patient's need.

Comparison of the MOST with earlier models

The classical model of medical diagnostic reasoning[18] is based on a 4-step process that includes collection of data, generation of hypotheses, interpretation of cues, and evaluation of hypotheses. This hypothetico-deductive model was designed to reflect the practice of medicine, but has often been used in nursing. The MOST is an analytic model, reflecting a logical thought process that can be examined as the decision-making process takes place.[19] Including the concept of sequential trials adds to the linear hypothetico-deductive model by introducing an element of circularity. This element allows introduction of new data as patterns continue to evolve and pattern recognition is refined.

Support for the MOST in the nursing literature

Several findings in this research are supported by the nursing literature. For example, nurses in this study preferred to delay using analgesics until they had tried alternative modalities. While not consistent with current recommendations for best practice,[3,20] the notion of "Medication as last resort" is consistent with research describing the nursing management of pain in children. Nurses were found to delay administration of analgesics as long as possible because they believed that drugs were harmful or had undesirable effects.[21] That nurses do not describe the use of a formal routine for making nursing decisions has been well described in the literature.[17] For example, research has shown that nurses believed relying primarily on intuition when assessing pain of cognitively impaired persons while they were actually performing a complex analysis of verbal and nonverbal cues.[22]

This work is consistent with the notion that the therapeutic trial is a necessary approach to the challenge of the resident's behavior (eg, agitation, restlessness, grimacing, calling out) that can represent discomfort[1] (eg, pain, constipation, hunger, emotional distress). The nurse must provide an intervention and assess the resident's response in order to fully determine the resident's needs.

Limitations

The study is limited by geography to the northeast United States, and by sample size. The key informant approach, however, by definition, does not require a large sample size. Each key informant is selected because he or she provides vital and crucial information. The research assumes that the key informants remember their experiences reliably and provide accurate information. Because the researcher knew the key informants prior to the beginning of the study, there lies the possibility of bias.

There are difficulties in any study of pain behavior. It is impossible to objectively validate pain behavior or to establish its reliability in any statistically significant way. This was a critical decision point for the nurses in this study. Nurses believed that their assessments of the resident's pain behavior were clinically significant and meaningful. During the treatment and evaluation process, pain behavior may change for reasons unrelated to pain. For example, pain behavior may diminish because the person is fatigued. It may increase because of anxiety or delirium. The person may become unable to demonstrate pain behavior because of progression of the illness or dying trajectory. Thus, while this model is suitable for use with persons who are nonverbal, other models will be necessary for persons who do not demonstrate measurable TPBs, for example, those who are comatose.

Recommendations for practice

In using this model, nurse should be open-minded and think creatively when choosing a target behavior. The literature suggests that residents may have unique behaviors that they demonstrate when they have pain. It is important for the nurse to know the individual resident as well as the geriatric nursing.[23,24] Diagnoses and treatment plans should be tailored to residents' preferences, sensory abilities, and current needs for social contact, stimulation, rest, and meaningful activity.[25]

Nurses should carefully observe and thoughtfully intervene in residents with pain history, functional disability, agitation, aggression, and depression.[25-27] While not explicitly included in the model, new behaviors may emerge at any time. Nurses should consider these new behaviors as evidence of insufficient/incorrect treatment or incorrect/incomplete diagnosis.

Recommendations for future research

The model, as described here, is specific to the problem of pain in cognitively impaired persons who live in nursing homes. Future work should evaluate the quality of decision making that results from the application of the model. Decisions should be evaluated for their empirical accuracy, internal consistency, and logic.[28] Further research should evaluate the model itself for communicability, context specificity, applicability, and the presence of excessive simplicity or reductionism.[28] Future research is needed to judge the applicability of this model in describing clinical decision making by nurses in other settings, working with other conditions, and with other symptoms. Usefulness of the model in teaching clinical decision making to staff nurses and advanced practice nurse practitioners should be evaluated.

TIPS FOR CHOOSING A TREATMENT MODALITY

- Note the resident's previous experience with a treatment modality
- Individualize application of the modality
- Treat in anticipation of a pain-producing event
- Use both drug and nondrug approaches

SUGGESTED TARGET BEHAVIORS

- Decreased functional status
- Impaired mobility
- Depression
- Decreased socialization
- Sleep disturbances
- Restlessness
- Decreased self-care
- Poor appetite
- Wandering
- New onset of incontinence
- Insistence on leaving the facility
- Disruptive behavior

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Utilization of comprehensive geriatric assessment in cancer patients

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Abstract

A growing and diverse aging population, recent advances in research on aging and cancer, and the fact that a disproportional burden of cancer still occurs in people aged 65 years and older have generated great interest in delivering better cancer care for older adults. This is particularly true as more survivors of cancer live to experience cancer as a chronic disease. Cancer and its treatment precipitate classic geriatric syndromes such as falls, malnutrition, delirium, and urinary incontinence. Comprehensive Geriatric Assessment (CGA), by taking all patient's needs into account and by incorporating patient's wishes for the level of aggressiveness of treatment, offers a model of integrating medical care with social support services. It holds the promise of controlling health care costs while improving quality of care by providing a better match of services to patient needs. Three decades after the CGA was initially developed in England, oncologists have begun taking notice on the potential benefits that CGA might bring to the field of geriatric oncology. This article describes the utilization of the CGA in cancer patients with an eye toward promoting interdisciplinary care for older cancer patients. To set an initial context, a search of computerized databases took place, using "comprehensive geriatric assessment" and "cancer" as keywords. A selection of literature from between 1980 and 2003 was reviewed. Additional articles were identified through the bibliography of relevant articles.

Keywords: Comprehensive geriatric assessment; Cancer; Older adults; Quality of life

1. Historical background

Comprehensive Geriatric Assessment (CGA) has been defined as a "multidisciplinary evaluation in which multiple problems of older persons are uncovered, described, and explained, if possible, and in which the resources and strengths of the person are catalogued, need for services assessed, and a coordinated care plan developed to focus interventions on the person's problems [1]". CGA extends beyond the traditional medical evaluation of older adults' health to include assessment of functional, cognitive, social, affective, economic, and environmental status as well as a discussion of patient preferences regarding advance directives [2]. The assessment also searches for common geriatric conditions that affect older adults' health and well-being, including impaired vision, hearing, mobility, falls, malnutrition, polypharmacy, depression, and urinary incontinence.

In the early 1970s, the framework of CGA was first utilized by Dr T.F. Williams as an outpatient screening tool for nursing home placement. Dr Williams and his colleagues found that CGA was effective in determining the avoidable nursing home placement for older adults [3]. Since then, CGA has grown in importance in the United States and around the world. The classic work was done by the team of Dr Laurence Rubenstein, as the first randomized clinical trial of an inpatient geriatric evaluation unit to test the effectiveness of a CGA-based program [4]. The results demonstrated that older patients receiving care in the geriatric evaluation unit were less likely to be discharged to a nursing home, more likely to have fewer nursing home days and retain gains in functional status than the patients who received usual care. One-year mortality and hospital admissions were also higher in the control group. The study population was targeted on older patients who expected to have a delay in discharge from a Veterans Affairs (VA) hospital [4]. The early success of CGA generated great interest and extensive support for research, education, and clinical practice. Subsequently, geriatric evaluation and management units (GEM) were developed at VA Medical Centers. Over the years, CGA has become a fundamental principle of geriatric health care because the delicate complexity of older adults, often with multiple chronic illnesses and limited reserves, requires a multidimensional and interdisciplinary approach to arrive at an optimal diagnosis and treatment plan.

2. Effectiveness of CGA in general

CGA has been extensively studied in various settings over the past 20 years, with conflicting results on outcomes. Well-designed studies have demonstrated the value of CGA in improving diagnostic and intervention outcomes in some settings, usually involving a geriatric interdisciplinary team approach and follow-up case management [5]. A meta-analysis in 1993, analyzing 28 clinical controlled trials of five types of geriatric assessment (inpatient CGA unit, inpatient CGA consultation service, in-home CGA, in-home CGA for discharged patients, and outpatient CGA) concluded that CGA programs that link geriatric assessment with strong long-term follow up and management are effective for improving survival and function in older adults [6].

Subsequent researchers seemed to support the notion that the more intensive the CGA intervention and the more control the geriatric team has over patient care, the more likely CGA will have a beneficial effect on disability and medical-related outcomes. Conversely, studies that involved only a single geriatric consultation service, no intense collaboration and follow up between the geriatric team and primary care providers, usually reported no differences in patient health status and related outcomes [7]. This may, at least partly, explain the reasons why most of CGA clinical trails delivered as consultation services in the community outpatient settings have little or no effect on subsequent patient function or survival. Lengths of follow up management and the adherence to geriatric recommendations, from the primary care providers as well as from patients, appeared

to be a significant factor for determining the effectiveness of CGA services. Continuity of care, in which patients are continuously reassessed and managed by an experienced interdisciplinary team, is emerging as an important factor in the care of older adults. Additionally, CGA is a diagnostic, not a therapeutic, intervention, and by itself cannot cure chronic illness or reverse disability. Only when CGA is accompanied with well executed targeted interventions and individualized care plans, improved patient outcomes can be expected.

Without a doubt, geriatric practitioners have learned a great deal from the research efforts put forth to date. Inpatient geriatric units, on-going CGA services in a hospital setting, and only intensive, extended, and well-targeted CGA services in outpatient clinics or community settings have proven to be effective in terms of functioning, nursing home placement, mortality, and some aspects of quality of life. Such interventions increase the overall quality and cost-effectiveness of care, in essence decreasing the need for more costly care in the future.

Although previous evaluative studies of CGA have focused on a limited set of outcomes related to functioning, health care utilization and costs, researchers and practitioners should start to take patients' and care givers' goals of care into consideration. One recent study interviewed patients and their caregivers that received care in an outpatient CGA setting regarding their goals of care. The most common categories of goals expressed by caregivers were obtaining education and referrals (57.5%) and improving social and family relationships (53%). The process of establishing and meeting such goals should be explicitly included in the design of future CGA evaluation studies [8]. Additionally, appropriate measures of the value of CGA service is the opinion of those who receive it. The physicians, nurses, family members, and patients may well see value in the way a geriatric team helps with complicated geriatric syndromes such as falls, incontinence, complex drug interactions, and mental status changes [9].

3. Application of CGA in cancer management

CGA has been suggested to be most beneficial when performed on older adults who are in transition (e.g. discharged from hospital, to nursing home, etc.), have recently developed physical conditions or impairments, and when specialty medical care is fragmented [1].

Multidimensional assessment such as CGA can be a tool to appreciate a holistic view that is often espoused, but frequently ignored in acute phases of cancer management. Aspects of CGA can be prioritized as indicated. Choosing an aspect of CGA to use with a particular older adult patient should be based on that individual's needs and acuity. For example, an acutely ill patient may best be served with a limited CGA that includes assessment of advanced directives and symptom distress. A more complete CGA would be indicated for the patient who is less acutely ill and anticipating return to home.

Table 1
Criteria for frailty

(Meets any one of the following criteria)
Cerebrovascular accident
Chronic and disabling illness
Confusion
Dependence in ADL's
Depression
Dementia
Falls
Impaired mobility
Incontinence
Malnutrition
Polypharmacy
Pressure sore
Prolonged bedrest
Restraints
Sensory impairment
Socioeconomic/family problems

When linked to therapeutic interventions and social supportive services, CGA can also help reduce the level of caregiver burden commonly experienced by family members of frail older adults with cancer. It is not yet categorized, in oncology practice, which should be the target population for CGA. Chronological age certainly should not be the only criterion. The general agreement exists that a CGA works best when targeting "frail" patients. Unfortunately, there are many operational definitions for frailty. Often the term "frail older adult" is used to denote those living in institutions or with impaired functional status. This makes the difference between frailty and functional dependence unclear [10]. Buchner and Wagner defined frailty as a state of reduced physiological capacity associated with increased susceptibility to disability [11]. Researchers with different outcomes of interest in mind have proposed several operational definitions of frailty. Most of those definitions have been centered on functional status and the presence of geriatric syndromes such as malnutrition/weight loss. Although there is no consensus as which definition will work best within the context of geriatric oncology, several researchers in the field have proposed to use the criteria that was developed by Dr Winograd and her colleagues (see Table 1). Those criteria of frailty have been demonstrated to be predictive of 1-year mortality and nursing home utilization in a cohort of 985 VA male patients [12]. However, the utilization of this definition for screening older patients with cancer for an in-depth CGA remains to be seen.

4. Cancer center-based CGA

The CGA has been used in some cancer centers in the United States and Europe. The center has typically estab-

Table 2
Seven major domains for CGA

Major domains	Common assessment tools
Medical assessment	See Table 3 for comprehensive listings
Functional assessment	Functional status
	Katz index of ADL[a]
	Lawton scale of IADL[a]
	ESDS
	ECOG-PS instrument[a]
	Comorbidity
	Charlson Comorbidity Index
	CIRS-G
Cognitive assessment	Mental status/dementia
	MMSE
	SPMSQ[a]
	T&C test[a]
	Clock-Drawing Test
	Delirium
	CAM
Affective assessment	GDS[a]
Social assessment	Social support assessment
	Caregiving issues
	ZBI
	CRA
	Elder abuse and neglect
	Conflict Tactics Scale
	EAI
Environmental assessment	NSC-Home Safety Checklist[a]
	Transportation
Advance directives	

[a] Instruments most suitable for initial screening.

lished a multidisciplinary geriatric oncology team, which provides a wide range of geriatric assessments and interventions. This approach allows the detection of common geriatric conditions and targeted interventions and care plans can be provided, within the context of cancer management [13]. One recent study indicated that, on average, older women with early stage of breast cancer presented with six geriatric conditions, besides their cancer diagnosis. During the 6-month follow-up, CGA further identified the average of three new conditions, and many of these conditions had an interaction with cancer treatment [14]. The principles of CGA in cancer management are described in the following text and Tables 2 and 3 provide a glance of approaches used in seven major domains including medical, functional, cognitive, affective, social, environmental assessments and advance directives.

4.1. Medical assessment

In the case of geriatric oncology, it is important for clinicians to structure their medical assessments to include evaluations of pain, symptom distress, malnutrition, polypharmacy, visual, hearing, and mobility/falls risk as well as searching for common geriatric syndromes, such as urinary incontinence. Each of these areas of assessment is briefly discussed.

Table 3
Approaches for medical assessment within the context of CGA

Medical assessment domain	Common assessment tools
Pain	Verbally administered 0–10 scale*
	Verbal descriptor scale*
	Pain thermometer*
	McGill Pain Questionnaire
	Wisconsin Brief Pain Inventory
Symptom distress	Symptom Distress Scale
Malnutrition	Anthropometrics
	Body weight/body mass index*
	Triceps skinfold thickness
	Arm muscle circumference
	Involuntary weight loss per unit time
	Biochemical tests
	Urine creatinine
	TLC
	Serum total cholesterol
	Serum albumin
	Clinical assessment
	Dietary behavior assessment
	Multi-items instrument
	MNA
Polypharmacy	Look for the concurrent use of multiple medications, especially more than one from the same drug classification
Vision	Snellen eye chart
	Screening with any available print*
	If patient is unable to read print
	Test ability to count upraised fingers
	Test ability to see flashlight beam in the dark
Hearing	Whisper test*
	Audiometer
Mobility/falls	Domains
	Balance and gait
	Lower extremity strength
	Previous falling history
	Instruments
	"Timed get up and go test"*
	Performance-oriented assessment of mobility
	Morse fall scale*
Urinary incontinence	"During the past 12 months have you ever lost your urine and got wet?"
	"If yes, have you lost urine on at least six separate days?"

4.1.1. Pain

Pain is one of the most frequent and disturbing symptoms associated with cancer. Older adults, generally, are more likely to experience pain, less likely to complain of pain, and more likely to have pain unrecognized and untreated, especially if they have any degree of cognitive impairment [15,16]. Older adults with cancer pain rely heavily on family and informal caregivers; for those older adults and caregivers, pain can be a metaphor for death, resulting in increased suffering [17]. Accordingly, pain management should have a high priority in the care of cancer patients, at any age [18].

The most accurate and reliable evidence of the existence of pain and its intensity is the patient's self-report. Even older patients with mild to moderate cognitive impairment

can be assessed for pain with simple questions and screening tools [19]. A variety of pain scales have been accepted for use among older adults. A verbally administered 0–10 scale is a good first choice for measuring pain intensity in most older adults [20]. The clinicians should simply ask the patient "On a scale of zero to ten, with zero meaning no pain and ten meaning the worst pain possible, how much pain do you have now?" However, some older adults may have difficulty responding to this scale. Other verbal descriptor scales, pain thermometers, and face pain scales also have accepted validity in older population and may be more reliable in those who have difficulty with the verbally administered 0–10 scale. For a comprehensive assessment of pain, multidimensional scales with multiple items often result in more stable measures and evaluation of pain in several domains. For example, the McGill Pain Questionnaire has been shown to capture pain in terms of intensity, affect, sensation, location, and several other domains that are impossible to assess with a single question [21]. The Wisconsin Brief Pain Inventory also has been studied largely in cancer pain [22]. Unfortunately, little has been published on the psychometric properties of those multidimensional tools evaluated specifically in older population. Thus it is important to utilize a scale that is appropriate for each case and document and use the same tool with each evaluation. Assessment and treatment strategies need to be sensitive to culture as well as the values and beliefs of individuals and families. The American Geriatrics Society (AGS) recently published a guideline for the management of persistent pain in older adults, more detail information is available on the AGS website and related publications.

4.1.2. Symptom distress

Older adults may experience a number of symptoms associated with cancer and other comorbidities. Inadequate symptom control throughout the illness will not only produce suffering but may have an adverse effect on the course of illness [23]. Effort to control symptoms may not only improve quality of life, but could also have the potential to improve quantity of life [24]. In addition, older adults who are not beset by physical problems have more energy to deal with the myriad psychosocial issues commonly encountered throughout the trajectory of cancer. Therefore, WHO recognizes that a cancer control program should contain, in addition to primary prevention, early diagnosis, and oncological treatment, a fourth phase aimed at palliating symptoms and preventing suffering.

Symptom management is an ongoing process of assessment, intervention, and evaluation. Ongoing thorough assessment is needed to identify the etiology of the symptom and to achieve efficacy of treatment. The Symptom Distress Scale developed by McCorkle and Young has been widely accepted and used extensively [25]. The 13-item scale indicates the degree of discomfort reported by the patients in relation to perception of 11 symptoms: nausea, appetite, insomnia, pain, breathing, cough, fatigue, bowel movement patterns, concentration, outlook, and appearance. The scale has been tested with patients with serious medical conditions and has a reported Cronbach's alpha coefficient of 0.70–0.92 [26].

4.1.3. Malnutrition

Malnutrition is among the most serious manifestations of cancer and its treatments [27]. Cancer-induced malnutrition may be even more severe in older adults, as aging is associated with anorexia, impaired body energy regulation, and with altered body composition. Furthermore, a large proportion of the aging population is at risk for malnutrition in the absence of cancer. Studies have shown that malnutrition is present in 10–51% of community-dwelling older adults, 20–60% of hospitalized older patients, and up to 85% of nursing home residents [28,29]. Age-related declines in body composition and cell function, complexity of multiple chronic illnesses, as well as the diverse dietary behaviors and cultural beliefs, make malnutrition in older adults more complicated and difficult to recognize [30]. The detection of malnutrition in older cancer patients should be included in routine assessment.

Several parameters including Anthropometric, Biochemical indicators, Clinical assessment, and Dietary intake evaluation (ABCD) have been used to assess the nutritional status in the aging population. It should be noted, however, no parameter or criterion has been accepted as the gold standard. They all suffer some shortcomings. Body weight, body mass index, triceps skinfold thickness, arm muscle circumference are the most commonly used anthropometric measures. The discriminant cutoffs for each measure continue to be disputed [29,31]. Weight loss per unit of time is believed to be a major indicator of malnutrition in older adults [32]. However, the literature is quite variable regarding the amount of weight loss and the unit of time that should prompt clinical investigation. An involuntary weight loss of greater than 5% within a 6-month period, especially when combine with muscle wasting, should raise medical attention. Cancer patients with an involuntary weight loss greater than 5% have a shorter median survival rate than cancer patients with stable weight. Patients with weight loss also respond poorly to chemotherapy and experience increased toxicity [33]. However, focusing on weight changes that might relate to hydration status in the critically ill could be misleading, too.

Biochemical tests that may reflect malnutrition are serum proteins, urine creatinine, immune function parameters (e.g. total lymphocyte count (TLC)), serum cholesterol, and leptin [34]. Serum protein levels are important markers of the body protein pool. Measurable proteins include albumin, transferrin, transhyterin (prealbumin), and others. Measurement of 24-h urine creatinine is the most frequently used biomedical index of muscle mass, which in turn might reflect nutritional status [35]. TLC has been utilized as a useful indicator of nutritional status and outcomes such as mortality. Serum cholesterol levels lower than 160 mg/dl

have been considered a reflection of low lipoprotein and thus of low visceral protein [36].

Serum albumin, alone or with TLC and cholesterol, is the most common used laboratory variable. Many researchers have questioned the value of albumin in diagnosing malnutrition in acute care settings. The long half-life of albumin means that even in those cases where malnutrition is the only factor causing albumin to fall, serum changes tend to occur late. This problem is not insurmountable as preabumin, a protein with a shorter half-life, can be substituted. A much more fundamental problem with the use of albumin as a defining criterion is the tendency for hypoalbuminemia to develop as the result of non-nutritional factors. The acute illness, trauma and sepsis can all have a direct effect on vascular permeability, leading to rapid hypoalbuminemia as proteins move into the interstitial space [37]. As to the dietary evaluation, 24-h or 3-day intake recall and food frequency questionnaires have long been criticized for its recalling bias as well as the complexity of administering in the clinical settings.

Owing to the unsatisfactory performance of a single measurement system for the assessment of nutritional status, particularly for the elderly population, attention has shifted to the use of a combination of these measurements to increase sensitivity and specificity. The Mini-Nutritional Assessment (MNA), an 18-item scale has demonstrated good validity and reliability in assessing nutritional status of older adults. It takes less than 15 min to administer and contains a substantial component of anthropometric measurements as well as sub-scales for dietary behavior, general assessment and subjective health [38]. Older adults are classified into three levels based on scores from 0 to 30: well-nourished (24–30), at risk for malnutrition (17–23.5) and protein-energy malnutrition (less than 17). The MNA also provides the clinician with the framework of nutritional assessments, thereby facilitating targeted interventions. The National Comprehensive Cancer Network has recommended the MNA for its clinical use [39].

4.1.4. Polypharmacy

Community-dwelling older Americans take an average of 2.7–4.2 prescriptive and over-the-counter medications [40]. Polypharmacy, a common occurrence in older adults with multiple chronic illnesses, is defined as the concurrent use of several different medications, including more than one medication from the same drug classification [41,42]. Problems associated polypharmacy include an increased risk of adverse drug reactions and falls among older adults. Studies have shown that the number of potential drug-related problems is associated to the total number of prescriptions [42]. Adherence also becomes difficult as the medication regimen becomes more complex. One common but often ignored consequence for polypharmacy is malnutrition induced by drugs [43]. Mechanisms of drug-nutrient interactions include reduced intake caused by side effects such as anorexia, nausea, vomiting, and altered taste perception. Furthermore, medications can interfere with nutrient absorption, cause alteration in nutrient metabolism and increase nutrient excretion [44]. Given the importance of proper nutrition as part of cancer management, every older adult should be told to bring in all current prescriptive and non-prescriptive medications, vitamins, and supplements for a review, as part of the assessment.

4.1.5. Visual and hearing

Vision impairment restricts activity, fosters dependency, and diminishes the sense of well-being in older adults [45]. Age-related visual changes affect central visual acuity, peripheral vision, contrast sensitivity, and color vision. The most common cause of blindness or visual impairment is age-related macular degeneration. Two common visual conditions, cataract and glaucoma, are essentially preventable causes of blindness [46]. Several community studies have found that visual impairment predicts functional disability among older adults and leads to high levels of handicap and emotional stress [47–49]. Visual impairment is related to increased morbidity. Those with visual impairment have an increased risk for falls, hip fractures, physical disability, and depression [50–52]. Hearing impairment, particularly that caused by presbyacusis, is the most common disorder affecting older adults [53]. The mental and cognitive health, social isolation, quality of life, and functional impact of hearing impairment has been demonstrated in numerous studies [54–57]. Older adults may decrease social interaction due to visual and hearing losses and this may further decrease their access to care. Given that some vision and hearing impairments are treatable, systematic screening of vision and hearing loss should be undertaken.

To test visual acuity, clinicians can use a Snellen eye chart, which requires patients to stand 20 feet from the chart and to read letters. A special hand-held card that simulates a Snellen chart, held 14 in. from the patient's eye, can also be used to identify visual impairment. If no charts are available, screen visual impairment with any available print. If patients cannot read even the largest letters, test their ability to count the upraised fingers and distinguish the flashlight from dark [57].

For hearing screening, a whispered test can be administered quickly. Further evaluation is indicated for those who can not repeat 50% of the whispered words correctly [58]. Ear toxicity has been reported in the use of some medications frequently associated with chemotherapy. In such cases, hearing assessment should be executed periodically with more accurate devices such as the Welch Allyn Audioscope, a hand-held otoscope with a built-in audiometer [2].

4.1.6. Mobility/falls

Mobility, the ability to get around in one's environment, is a function composed of multiple maneuvers. Many people experience a decline in mobility with aging. A cancer diagnosis, multiple co-morbidities, and aging changes responsible for this decline also may predispose patients to falling.

Falls are a major cause of mortality, morbidity, functional impairment, and nursing home admission among older population [59]. Accordingly, the assessment of risks for falling is undertaken by assessing balance, gait, lower extremity strength, and a pervious falling history. As a beginning step, the assessment of fall risk can start with a simple question. Studies have demonstrated that a screening question "During the past 12 months have you fallen all the way to the ground or fallen and hit something like a chair or stair?" had a sensitivity and specificity of 86.4 and 66.1%, respectively, for being a clinically, meaningful problem confirmed by an in-depth CGA [60]. Besides a careful and well-directed history regarding fall incidents, gait and balance should be assessed by direct observation of older patients rising from an arm chair, walking 10 feet, turning around, walking back and siting down again. This "Timed Up and Go Test" is designed as a timed measure. Older adults who take more than 20 s to complete the task require further evaluation [61].

The performance-oriented assessment of mobility instrument is a standardized and more extensive assessment tool evaluating the quality of the complex activities of standing and walking [62]. A score below 20 points, with a maximum of 28, indicates an impaired gait, and therefore, an increased risk of falling. The performance-oriented assessment has provided a means of measuring mobility in many research and clinical settings. Once clinicians become familiar with the principles of these assessment tools, they can quickly perform a gait and balance assessment by observing patient's movements during a busy office visit.

Another widely used instrument, the Morse fall scale, is designed to be a simple and quick tool administered by nurses. Six items identify patients at risk for falling, includes history of falling, secondary diagnosis, ambulatory aids, intravenous therapy, gait abnormalities, and mental status. The summed and weighted scores ranged from 0 to 125, with higher scores indicate higher risk for falling. Validity and reliability have been established. Once the nurse is trained, the scale takes less than 3 min to complete [63].

4.1.7. Urinary incontinence

Urinary incontinence is distressing to patients and to their caregivers. It may be the result of cancer and its treatment. Difficulties in managing urinary incontinence contribute to the decision to institutionalize the geriatric patient. The prevalence of any degree of incontinence in community-dwelling older adults is between 15 and 30%. Urinary incontinence is about twice as prevalent in older women as in older men [64]. As people age, physiological changes occur that predispose individuals to urinary incontinence. However, incontinence or leakage of urine should not be thought of as a normal process of aging. Studies have demonstrated that urinary incontinence is associated with a constellation of physical and behavioral factors that can impose a social and emotional burden. Even though the impact of incontinence is highly variable, and it depends upon the individual [65], clinicians must screen for this common geriatric syndrome, ask older patients about the impact of urinary incontinence, and be prepared to offer treatment when patients request.

Two simple screening questions, "During the past 12 months have you ever lost your urine and got wet?" and "If yes, have you lost urine on at least six separate days?", have demonstrated good sensitivity, specificity, and positive predictive value in clinical studies [66]. Answering "yes" to both questions indicates a potential problem with urinary incontinence that needs further evaluation. Referral to nurse-managed continence programs or urologists can be arranged, if needed.

4.2. Functional assessment

Functional assessment is a cardinal component of geriatric care. In many respects, the older adult's ability to function is among the most important measures of the overall impact of illness. Functional status and comorbidity/physical burden of illness should be assessed routinely.

4.2.1. Functional status

Cancer is considered catastrophic in nature because it necessitates major changes in the living pattern of adults with cancer. Such changes are characterized by physical alterations in the body that over time impinge on the patient's ability to function as a normal social being and lead to a state of enforced social dependency. Such enforced social dependency threatens the person's independence or autonomy and potentially may decrease one's sense of power, control, and self-esteem. Not only does this increased dependency impinge negatively on the patient's self-esteem, but also social relationships may be dramatically altered.

The first and most frequently used scale to measure physical competence, the Katz index of Activities of Daily Living (ADL) assessing the patient's need for assistance in bathing, dressing, eating, transfer, toileting and continence [67]. In addition to ADL, another set of activities required for independent living are the Instrumental Activities of Daily Living (IADL), including the abilities of using the phone, traveling, shopping, preparing meals, doing housework, taking medications and managing money [68]. Both scales have demonstrated good reliability and validity in the older population. Several studies have also indicated that ADL and IADL scales are more sensitive in the older cancer population than the conventional functional assessment such as Eastern Cooperative Oncology Group Performance Status [69]. Additionally, the items of ADL and IADL translate readily into services. Information of the physical competence of the older adults with cancer becomes an indicator of what services might be needed.

Although physical competence is the center of attention for most studies, social competence, such as loss of social interest and role activity that accompany cancer diagnosis, retirement, death of family or friends, should not be discounted. Inability to maintain older cancer adults' social

competence due to diminished physical ability is one aspect that has not been explored. Most recently, there have been efforts to expand research in this area. Jepsen, Schultz, Lusk and McCorkle examined the relationship of physical and social dependency, measuring by Enforced Social Dependency Scale (ESDS), with cancer survival and found that ESDS score contributes significantly to the model of survival time [70]. The ESDS measures personal and social competence. Personal competency includes six activities: eating, dressing, walking, traveling, bathing, and toileting, rated by the interviewer on a 6-point scale. Social competence includes home, work, and recreational activities, rated on 4-point scales, and communication, rated on a 3-point scale. Scores for personal and social competence were summed to produce a total dependency score ranging from 10 to 51, with higher scores reflecting greater dependency [71]. Reliability and validity of the ESDS also has been well established [72].

4.2.2. Comorbidity

The construct "comorbidity" reflects the aggregate effect of all clinical conditions a patient might have, excluding the disease of primary interest [73]. Comorbidity is independent from functional status, and therefore, can provide additional prognostic information in older adults with cancer [74]. An Italian study suggests that comorbidity measured by the Charlson index has as much influence as functional status on the tolerance of chemotherapy as well as on survival [75]. Several studies have shown that survival of patients with solid tumors such as breast, colon, prostate and head and neck cancers is significantly modified by comorbidity [76]. Conflicting results also exist, comorbidity measured by the Charlson index and Cumulative illness rating scale-geriatrics (CIRS-G) did not emerge as a predictor on the tolerance of chemotherapy in one recent prospective pilot study [77].

The role of comorbidity in cancer management and decision making is just beginning to be explored. Because there is no "gold standard" for measuring comorbidities, researchers have validated measures of comorbidity by how well they predict mortality, health care utilization and other health-related outcomes. Several well-known weighted instruments, such as the Charlson Comorbidity Index and CIRS-G, have been proposed to assess comorbidities, although none have been validated or widely accepted for use in older adults with cancer [76]. It is important to note that the Charlson and CIRS-G provide a very different qualitative and quantitative view of comorbidity in the same collective. The correlation between the Charlson and CIRS-G was reported between 0.39 and 0.51 in two studies [74,78]. Therefore, the choice of a scale is not straightforward and results should always be interpreted with caution.

4.3. Cognitive assessment

Cognitive impairment is common among older adults, but individuals with dementia or other types of cognitive impairment frequently go unrecognized. Assessment of cognitive status is essential to detect unsuspected mental status changes and to provide a basis for comparison in future encounters. It should be emphasized that the possibility of cognitive changes secondary to primary or metastatic brain tumors should always be excluded [18].

4.3.1. Mental status/dementia

The complete mental status examination encompasses an assessment of the level of consciousness, attention, language, memory, proverb interpretation, similarities, calculations, writing, and constructional ability [79]. A number of scales have been utilized to assess mental status and screen for dementia. The Folstein Mini-Mental State Examination (MMSE) is one of the mostly widely employed tests of cognitive assessment, and is one of the most studied [80]. However, MMSE has been reported to be heavily influenced by education level and socioeconomic status and it also has limited sensitivity for early stage of dementia. Several other scales also have been validated including the Short Portable Mental Status Questionnaire (SPMSQ), the Time and Change (T&C) test, and Clock-Drawing Test.

The SPMSQ, one of simpler and widely used scales developed by Pfeiffer, comprises ten questions dealing with orientation, personal history, remote memory, and calculations [81]. Although SPMSQ is easy to administer and appears to be less affected by ethnicity and educational level, studies also have demonstrated that there are many false-negative results with SPMSQ. When administered to community-dwelling older adults, the specificity is found to be better than 90%, the sensitivity, however, may be as low as 50% [82,83]. If one wished to detect as many cases of dementia as possible for future assessment, more stringent tests might be used. In contrast to SPMSQ, the T&C Test is another simple screening test aimed to maximize sensitivity and negative predictive accuracy, in turn minimizing false-negative results. The T&C test is a performance-based tool that dealing with telling time and making change, two simple tasks that are crucial for maintaining independent functioning. In the telling time task, patients must respond to a clock-face set at 11:10 h. Time to response is measured with a stopwatch. The patient is allowed two tries within a 120-s period. In the making change task, three quarters, seven dimes, and seven nickels are placed in front of the patient. The patient is cued to give 1$ in change. The patient is also allowed two tries within 120-s period [84]. The T&C test had a sensitivity of 86%, specificity of 71%, and negative predictive value of 97%. Strong convergent validity is demonstrating by high correlation with MMSE ($r = 0.58$). The T&C test took a mean of 22.9 s to complete and education explained only 3% of score variance, compared with 13% of MMSE [84].

In the Clock-Drawing Test, the patient is presented with a pen and a piece of paper on which a 4–6 in. circle is drawn and asked to write the numbers and draw the hands of clock to show 10 past 11 [85]. Many scoring and administering

systems for the Clock-Drawing Test have been suggested, but none is standard or has gained wide acceptance yet. It is important to note that all those scales are designed as screening tools, further evaluation should be warranted when a positive screening is indicated.

4.3.2. Delirium

Delirium is a common geriatric syndrome and should be considered whenever a change in behavior or cognition is evident. The hallmarks of delirium are acute onset, fluctuating course, impaired attention, cognitive changes, and medical causation [86]. As health care continues to shift away from hospitals, delirium is increasingly a common outpatient problem. Delirium is often mistaken for dementia, depression, and other psychiatric disorders. The Confusion Assessment Method (CAM) is an easy, four-step algorithmic diagnostic test, which can be complete by a clinical evaluator who is nonpsychiatrically trained [87]. The CAM has been widely used and validated as a clinical instrument for assessing delirium and it has been translated into three languages [88].

4.4. Affective assessment: depression

Affective assessment is particularly important in older adults with cancer, given that a diagnosis of cancer and the excess burden of cancer management may lead to depressive symptoms. Depressive symptoms have been associated with physical decline and weight loss in older adults [89–91]. In older adults with depressive symptoms, about 90% lose weight compared with 60% of younger persons with depressive symptoms [92]. Refusal to eat can be a suicidal gesture. Depression is associated with increased cerebrospinal fluid concentrations of corticotropin releasing factor, a potent anorectic agent [93]. Those complications of depression may compromise the outcome of cancer management. It is important to note that all patients facing a progressive disease will undergo a process of normal grief and bereavement, which includes feelings of sadness, anger, and self-doubt. However, the clinician must have a high index of suspicion for signs of clinical depression, which place older patients at risk for increased suffering, as well as cognitive and functional declined [94].

Screening for depressive symptoms can be achieved using a simple tool such as 15 or 30-item Geriatric Depression Scale (GDS). The Institute of Medicine has recommended the GDS for clinical use. Using a cutoff score of 11 or above for the 30-item scale, the scale is 84% sensitive and 95% specific for diagnosing clinical depression [95]. Dr Balducci and Dr Beghe have reported that when using the GDS, they have diagnosed depression in more than 20% of their older patients with cancer, and in half of these patients, depression would have been missed without the GDS [96]. Given the consequences of depression and its reversibility, screening for depressive symptoms should be part of the assessment in caring older patient with cancer.

4.5. Social assessment

4.5.1. Social support

Social support, along with retention of a sense of personal autonomy and control, is mentioned specifically as one of the key ingredients in successful aging [97]. An increase in social interaction at meal times has been shown to improve dietary intake [98,99]. Social support, therefore, can play an important role in nutrition and health [100]. Social support also has been linked to mortality, however, the definition of social support has an important effect on the relationship found [101]. Blazer examined a large group of older adults and found social support to be a significant factor for 30-month mortality [102]. However, the magnitude depended on the definition of support. A measure of perceived available support was more strongly related to mortality than either support defined as a frequency of interaction or in terms of availability of roles and attachment (e.g. marital status, number of children, etc.).

The assessment of social support can be conducted in a structured manner through the use of a variety of instruments or through a more informal means by asking a series of questions aimed at gathering information about who provides help and support to older adults with cancer. Despite a considerable body of literature, little consensus has been made toward identifying a gold standard to measure social support in the aging population. Selection of instruments is no easy task and the results should be interpreted with caution. Informally, the clinician can probe systematically about the assistance being provided through the social network of older adults. For many frail older adults with cancer, the availability of assistance from family and friends informs the decision about the cancer treatment strategy. The periodic assessment of social support allows the clinician to detect changes in care needs, to devise tailored interventions and to prevent burn-out of caregivers [18].

4.5.2. Caregiver burden

The trend toward shortened hospital stays implies an increasing reliance on families to take care of older cancer patients. Providing care to older cancer patients at home does come with significant challenges and potential consequences for families. While many caregivers value their caregiving role, they achieve patients' preference of staying at home with their own emotional and physical sacrifice as well as profound economic difficulties for an undetermined length of time. Stommel, Given and Given reported that family caregivers spent 4.7 h/day on average in providing direct care to cancer patients at home [103]. Results from the SUPPORT showed that by the time the seriously ill patient had died, in more than 40% of cases, a family member had to quit work or make another major life change to provide care for the patient. Nearly one-third of families lost a major source of income and 25% of families lost most or all of their family savings. The inability of caregivers to meet

patients' needs for daily assistance may compromise cancer patients' physical well-being and result in unnecessary hospitalization [104].

Given that caregiver burden is linked with cancer outcomes, and that many caregivers are over 65 themselves, assessing caregiver burden is warrant. The Zarit Burden Interview (ZBI) is the instrument most consistently used in dementia caregiving research [105]. The ZBI a 22-item scale designed to assess the extent to which caregivers of older adults perceive their roles and responsibilities as having adverse effects on their health, life and well-being [106]. Another available scale is the Caregiver Reaction Assessment (CRA), a 24-item instrument assesses the reactions of family members caring for older adults with physical impairments, Alzheimer's disease and cancer [107]. Both scales have reported satisfactory psychometric properties. Despite the initial evidence supporting the linkage of caregivers' well-being with some aspects of patient outcomes, there is an urgent need to further evaluate how caregiver burden impacts on the pattern of health care resource utilization and older cancer patient outcomes, including adherence to treatment, survival, and quality of life.

4.5.3. Elder abuse/neglect

Older adults with cancer might be vulnerable to elder abuse/neglect given their elevated caregiving needs and uncertain progonisis. The true prevalence of elder abuse is difficult to determine because there is great variation among states regarding what constitutes elder abuse. Conservative estimates indicate that 1.3% of the nation's older adults are victims of abuse each year, with only one in 14 elder abuse cases reported to a public agency [108]. Adult Protective Service (APS) Department indicated that the most common form of reported elder abuse was neglect, accounting for 55% of cases. Sixty-two percent of cases involved abuse by other people, whereas 38% involved self-neglect. Ninety percent of the perpetrator was a family member. The majority of victims are female (67%) and Caucasian (66%).

During a visit, some behavioral and physical signs should raise suspicion for elder abuse, including fearfulness toward the caregiver, poor eye contact, a hesitation to talk openly, poor hygiene, weight loss, hematomas, bruises, pressure sores, or multiple fractures in various stages of healing [109]. Other indications of possible abuse may include confusion, paranoia, anxiety, anger, or low self-esteem [110].

As with other aspects of social assessment, assessment of elder abuse may be accomplished with the use of formal instruments. For example, a modification of the Conflict Tactics Scale can be used to assess elder abuse [111]. Additionally, Elder Assessment Instrument (EAI), a 44-item Likert scale can be performed quickly [112]. This instrument is comprised of seven sections that reviews signs, symptoms and subjective complaints of elder abuse, neglect, exploitation and abandonment. The EAI is reported to be highly sensitive, less specific, and it takes approximately 12–15 min to administer [113].

4.6. Environmental assessment: home safety and transportation

Environmental assessment encompasses two major domains: home safety and transportation/access to care. The National Safety Council has developed a Home Safety Checklist that older adults and their caregivers can self assess. Particularly, for older adults who are at risk for recurrent falls, a home health nurse can be sent to inspect homes for safety and the recommendation of installing devices, such as raised toilet seats and shower bars, can be made. Transportation needs may be exceptionally important among older adults with limited physical and social capacities.

4.7. Advance directives

Advance directives, a general term that describes two kinds of legal documents, are living wills and medical powers of attorney. These documents allow a person to give instructions about future medical care should an individual be unable to participate in medical decisions due to serious illness or incapacity. Discussions of advance directives are particularly important for older adults who have life-threatening malignancies. However, clinicians need to make it clear that discussions of advance directive do not equate to stopping treatment. Preferences for aggressive cancer treatment and preferences for advance directives are two different and separate issues. As such, discussions regarding advance directive need to begin early in the course of treatment rather than the days when incapacity or death is imminent.

5. Office-based CGA

The expansion of capitated Medicare programs, shorter length of hospital stay, and the chronic nature of cancer management have shift the focus of CGA from hospital settings to primary care clinics. When seeing an older adult with cancer, especially those with multiple chronic illnesses, primary care providers face the daunting task of completing a comprehensive evaluation in a timely and efficient manner. The application of valid assessment tools widely used in a CGA is a feasible means of performing a multidimensional assessment in an office setting. Simplified screening tools and questions would facilitate incorporating a CGA into a busy oncologist's office. Screening guidelines were recently published by the National Comprehensive Cancer Network [13] (see Table 4). These guidelines may first appear minimal, but will develop as more research data specific to older cancer patients emerge from future oncogeriatric studies.

Several CGA studies have utilized simple screening questions to expedite the rapid screening of older patient in the private practice office [60,66,114]. Typically, these screening instruments take between 5 and 15 min to complete,

Table 4
Selected GSA screening and assessment guideline recommended by NCCN

	Screening	Assessment
Mental status	Serial three: tell patients, "I am going to name three objects and I am going to ask you to repeat them now and a few minutes from now"	Folstein Mini-Mental Status, if score <24, institute work-up for dementia
Emotional status/depression	Ask patient, "do you often feel depressed or sad?"	GDS, if score >10, work-up for depression
ADL	Can you dress yourself? Do you need help to go to the bathroom? Do you wet yourself? Can you eat without help? Can you move from one place to another without help? Do you need help taking a bath or a shower?	Katz ADL scale
IADL	Do you drive? Are you able to use public transportation? Do you prepare your own meals? Do you go shopping? Do you do your own checking? Can you call someone with the telephone? Do you remember to take your medications?	IADL scale
House environment	Do you have trouble with stairs inside and outside the house? Do you trip often on rugs?	
Social support	Who would be able to help you in case of emergency?	If no caregiver, try to arrange for services; if caregiver is a spouse, a sibling, or a friend of the same age as the patient, assess independence of the caregiver
Comorbidity	Evaluate the presence of the following conditions from review of systems	Confirm the presence of the condition and grade the seriousness
Nutrition	Weigh patient, measure height, inquire about weight loss	MNA
Polypharmacy	Review number and type of medications	If >3, look for duplications, interactions, and compliance

depending on how comprehensive the screening domains are included. One study demonstrated that, when targeting four common geriatric syndromes including depression, falls, urinary incontinence, and functional impairment, a 15-item questionnaire that takes 5 min to complete had accuracy rates of 66.4, 69.1, 83.3, and 70%, respectively [66]. The positive predictive values of these four potentially treatment geriatric syndromes ranged as high as 92.7% for urinary incontinence to the lowest 30.7% for falls. These measures were comparable, if not better, than many widely used screening instruments for other medical conditions. For example, standard fecal occult blood testing for colon cancer has been reported to have positive predictive values of 5–10%, while mammography has been reported to have positive values from 5 to 38% [115,116].

The effective CGA should be viewed as a three staged process: (1) identifying or targeting appropriate patients, (2) assessing the patient and developing recommendations, and (3) implementing recommendations of health care providers and patients [66,117]. Obviously, time, training, and resources are heavily involved in this process. Outside of academic medicine and private philanthropy or government funding, most private offices under current Medicare fee-for-service payment system cannot afford to provide an extensive CGA by an interdisciplinary geriatric team. The CGA requires a methodological approach to GEM that can be learned by primary care providers (oncologists in this case) and accomplished over time in an office setting [5]. Future research with the use CGA with cancer patients is needed to address this issue.

6. Utilization of a CGA with cancer patients

Current development of incorporating a CGA in the management of older patients with cancer is still in its infancy stage. In younger adults, the Eastern Cooperative Oncology Group Performance Status (ECOG-PS) is a powerful predictor of therapeutic response, toxicity, and outcome. The prognostic value of PS, however, may fade with increased age [77]. In older adults with cancer, PS is likely affected by chronic illnesses and disability and may not reflect the impact of cancer. Thus PS appears informative in older adults without comorbidities, but is inadequate for the prognostic assessment of older adults with multiple chronic illnesses. Additionally, PS represents a clinician's viewpoint and does not account for the subjective psychosocial aspects of life, which assume greater importance in the aged [118]. Clearly, the heterogeneity of an older population is reflected in the multiple and different factors which may influence the final outcome of cancer treatment. The adoption of CGA, an uniform assessment of older adults, is essential to establish the prognostic value of different factors in treating older adults with cancer.

Standard use of instruments would facilitate the development of a common language of assessment, and thereby lead to improved communication among professionals caring for older adults. An Italian group for geriatric oncology study has attempted to standardize and validate a CGA based scale for use in older adults with cancer. The Multidimensional Assessment for Cancer in the Elderly (MACE) was developed to collect information on demographics, socioeconomic status, presence of major symptoms, comorbidity, use of services, cognitive status, depression, physical performance, disability, and tumor characteristics. The MACE includes many widely used geriatric scales, such as Mini Mental Status Examination, GDS, Gait and Balance Scale, Physical Performance Test, Katz ADLs Scale, Lawton's IADLs Scale, and World Health Organization Scale.

The MACE, on average, takes 27 min to administer. Both for inter-rater and test-retest reliability, the values of the intraclass correlation coefficient (ICC) were generally higher than 0.7, demonstrating good reproducibility. For test of concurrent validity, Sickness Impact Profile (SIP) was used as a reference measure. The results showed that disability (ADL, IADL, and WHO scores), cognitive status, depressive symptoms, and the number of days spent in bed sick in the last 2 weeks were markedly correlated with the global, physical and social SIP scores. Disability alone accounted for 70% of variance in the SIP global score, 83% in the SIP physical score, and 45% of the variance in the SIP psychosocial score. The authors concluded that the MACE is applicable as a clinical research tool to avoid arbitrary decisions on patient selection for enrollment in clinical trials, to favor uniform monitoring of treatment, and to allow a better comparison of results [119].

By selecting SIP as a reference measure against the MACE, the conceptual similarity of CGA and Quality of Life (QOL) assessment surfaces. There are many parallels between CGA and QOL assessment in that they are multidimensional and broad. Both utilize standardized instruments that frequently rely on patient perceptions and other "biologically soft" measures. Moreover, they share many dimensions and focus on issues that are among the most important to older adults, particularly the ability to function fully in social roles and participate in activities consistent with their desires. However, some differences between the two constructs illustrate that two are not synonymous [120]. For example, unlike QOL is best assessed by the patient, some dimensions of CGA, such as nutrition, gait and balance, polypharmacy, or cognitive status may be better assessed by clinicians or caregivers. Considerable opportunities exist for integration of CGA and QOL assessments. Knowledge gained by both areas will facilitate better care for the older adults with cancer.

Other researchers also have generated some fruitful results, beginning to demonstrate the utilization and effectiveness of CGA in adding valuable insight in predicting mortality and disability as well as informing treatment decision. Dr Repetto and his colleagues have shown that CGA adds substantial information on the functional assessment of older patients with cancer, including patients with a good PS. The MACE was administered in a group of 363 older adults with solid ($n = 271$) or hematological ($n = 92$) tumors, in addition to PS and Satariano's index. The results indicated that a statistically significant association emerged between comorbidity as measured by the Satariano' index and functional status by ADL and IADL. No association was found between PS and comorbidity, underlining the importance of comprehensive assessment of the global health status of older adults with cancer by means of CGA. Although PS was significantly associated with some CGA items, several aspects of functional impairment as measured by ADL and IADL were missed by PS: between 9 and 38% of patients with good PS (<2) had limitations detected by CGA. The authors suggested that ADL and IADL are more sensitive than PS alone. In particular, the IADL scale recognized the aspects of daily life that require instrumental activities, such as using public transportation, that may affect adherence to cancer treatment. Further studies are needed to assess whether a CGA can properly address the treatment decision making, treatment-related toxicity, and survival, thus helping to achieve a wider consensus on the instruments to be adopted [69].

7. Interdisciplinary geriatric oncology

The magnitude of the problem of cancer in old age has been widely stressed in the literature during the last decade. The scarcity of clinical research data, however, provides silent testimony that cancer in old age has not been given adequate attention. It is important to note that many impairments caused by cancers and their treatments precipitate typical geriatric syndromes such as falls, malnutrition, delirium, and urinary incontinence. These geriatric syndromes represent a hallmark of frailty. Thus, the oncology clinicians have a greater responsibility to be more familiar than other specialists with the multidimensional and interdisciplinary nature of CGA.

Health care has traditionally been multidisciplinary, with resources of several disciplines applied sequentially. An interdisciplinary approach recognizes that many clinical problems outstrip the tools of individual disciplines and entails several health care providers simultaneously and cooperatively to evaluate the patient and develop a joint plan of action. Interdisciplinary care is becoming common in many aspects of medicine, including geriatric, cardiac and cancer care. The issue of geriatric oncology is as complicated and elusive as the definition of aging, a highly individualized process involving changes in physical, physiological, social and economic domains. In the past years, geriatric oncology certainly has elicited more interest than ever before. The National Institute on Aging and the National Cancer Institute have issued a Request for Application (RFA) for the study directed at cancer in older adults. Research is sought on

early detection, diagnosis, prevention, treatment, prognosis and survival, and how age-associated problems affect these areas; a multidisciplinary working group is also convened by the National Institute on Aging and the National Cancer Institute; all major cooperative oncology groups have included committees devoted to the issue of geriatric oncology; the Hartford Foundation has initiated an innovative 6-year combined internal medicine residency and medical oncology geriatric training program; and the number of scientific articles concerning management of cancer in older adults has increased dramatically. Development of closer ties between oncology and geriatric clinicians will contribute to progress and collaborative success of cancer management in older adults.

In the cancer management of older adults, treatment outcomes should not only be measured by survival rates, but also by functional status and the resulting quality of life. In light of this, aspects such as maintaining independence, provision of nursing care and social services, or pain management deem greater significance. Underscoring these, it is evident that a CGA directed at older adults with cancer requires an interdisciplinary team approach for assessment and intervention.

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University of Connecticut Health Center

Office of the
Executive Vice President for
Health Affairs

Dean, School of Medicine

April 26, 2006

Dr. Amy Laufer Kenefick
School of Nursing
University of Connecticut
Storrs, CT 06269-3044

Dear Dr. Kenefick:

This will confirm that your joint appointment has been approved as Assistant Professor, in the Department of Medicine, University of Connecticut School of Medicine, effective April 1, 2006 through December 31, 2006.

You will retain your principal appointment with the University in the School of Nursing.

Sincerely,

Peter J. Deckers MD

Peter J. Deckers, M.D.
Executive Vice President for Health Affairs
Dean, School of Medicine

sas
cc: Dean's File
Department Head (primary and joint)
Human Resources File

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Associate Professor
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April 26, 2006

Dear Dr. Kenefick:

On behalf of the UConn School of Nursing, I am pleased to inform you of an award of $5,000 for your study entitled *Translational Research in Breast Cancer Survivorship*. Your work continues to be impressive and well supported by your peers.

I look forward to hearing of your findings, and encourage you and your student and agency partners to present the findings of this award at the 2007 Athena Research Conference, scheduled for April 19, 2007. We encourage participation in other local conferences such as ENRS; the conference is in Providence on April 12-14, 2007, as well as CT Sigma Theta Tau which is likely to be in March of next year. Please remember that a final report in publication format is due within one year.

If I or the Center for Nursing Research can be of further assistance, please let me know. Good luck with your study.

Sincerely yours,

Deborah Shelton

Deborah Shelton, PhD, RN, BC

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RELATIONSHIP OF NEUROCOGNITIVE FUNCTION TO BREAST CANCER TREATMENT AND INDUCED MENOPAUSE

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Introduction: Women who have received chemotherapy for breast cancer report difficulties with neurocognitive function (NCF), particularly memory and concentration. Characteristics and implications of these difficulties are not well defined. The symptoms that they report resemble symptoms reported by women who experience menopause. Some women who have chemotherapy also experience induced menopause. The role that induced menopause may play in altering NCF is unclear.

Purpose: (1) describe characteristics of NCF over time in women who receive breast cancer chemotherapy as compared to women who experience surgically induced menopause and (2) identify any relationships between NCF and symptom distress or functional status.

Procedures: The proposed research is a prospective longitudinal descriptive study of NCF in premenopausal women who received breast cancer chemotherapy compared to premenopausal women who experience abrupt induced menopause as a result of total abdominal hysterectomy/oophorectomy. Comparison of these two groups may clarify the contribution of chemotherapy and induced menopause to changes in NCF, leading to interventions that will contribute to overall well being during treatment and survival.

Instruments include an investigator-developed demographic and medical history form; the Wechsler Adult Intelligence Scale (WAIS-III); the Symptom Distress Scale (SDS); the Enforced Social Dependency Scale (ESDS); the State-Trait Anxiety Scale (STAI); and the Center for Epidemiological Studies Depression Scale (CES-D).

Data Collection Points are (1) baseline, before chemotherapy or surgery; (2) 6-8 weeks after initiation of chemotherapy or surgery; (3) 6 months after initiation of chemotherapy or surgery; and (4) 9 months after initiation of chemotherapy or surgery.

Analysis includes (1) Descriptive statistics to describe characteristics of the sample, characteristics of NCF, symptoms and functional status at each of the data collection points. (2) Inferential statistics to identify the longitudinal relationship of NCF and chemotherapy; identify the relationship between induced menopause and NCF. Compare NCF changes in breast cancer chemotherapy patients to hysterectomy/oophorectomy patients, identify relationships between NCF, symptom distress and functional status.

Results to date: This pilot study will include 25 women with breast cancer chemotherapy and 25 women with hysterectomy/oophorectomy but no chemotherapy. Data collection is under way.

Significance: The impact of persistent and late effects of therapy on the quality of life of the nearly two million breast cancer survivors is not fully known. As survival rates for women with breast cancer increase, so does the importance of considering quality of life outcomes of treatment. Results of this research will increase the understanding of the interrelationships between neurocognitive function, breast cancer treatment and induced menopause. Findings will influence the design of clinical trials and treatment protocols; the development of interventions to improve quality of life in women undergoing treatment for breast cancer; and improve the validity of the informed consent process by allowing the patient to be better informed about treatment side-effects.

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PROTOCOL SUMMARY

Mental and Physical Stressors in the Diagnosis of Breast Cancer: A Multidisciplinary Analysis of Distress and Systemic Biomarkers in Patients Referred for Biopsy of a Suspected Breast Cancer Lesion
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Background and Significance:

A. Symptom Distress:

Women begin to face their greatest fear when they have been told that their routine mammogram or breast exam is abnormal. Women experience an array of symptoms throughout the course of their diagnosis, treatment and recovery from breast cancer. These include anxiety, mood disturbances, fatigue, and difficulties with concentration (1-4). Sleep problems are also a commonly reported symptom among cancer patients as well. Symptoms are perceived indicators of change in normal functioning as experienced by patients (9). Symptoms disrupt daily functioning, most notably social function and communication. Symptom outcomes impact functional and emotional status, health care service utilization, mortality/morbidity, financial status, and self-are/management (10-13).

Research has demonstrated the presence of significant associations between symptoms experienced by breast cancer survivors, suggesting a complex web of symptom experience (12). The nature of the complex interactions between symptoms remains unclear. Patients with one symptom are likely to have others, as well. One of the major symptoms experienced by patients is cancer-related fatigue. Cancer-related fatigue (CF) is a multidimensional and multifactorial phenomenon. It can be readily differentiated from the fatigue experienced by healthy individuals (14). It presents as an unusual, persistent sense of tiredness that frequently occurs with cancer and cancer therapy (15) and it is unrelieved by rest or additional sleep (16). As CF is a more severe, energy draining, and unrelenting type of fatigue (17), it impacts both physical and mental capacity and has devastating effects on many aspects of patients' lives. The profound effects of fatigue and depression are very difficult for patients to communicate to those who take care of them including their families, friends and health care providers. Communication about this experience is further complicated by the lack of appreciation of those around the patient (18). The National Institutes of Health (NIH) convened a 'State-of-the-Science' conference on cancer symptom management in 2002 to address the quality of life issues in cancer patients. The authors of this conference acknowledged cancer-related fatigue, depression and pain as the most frequent and the most debilitating symptoms of cancer and cancer treatments (19). A number of cross-sectional studies have identified a strong correlation between fatigue and depression (20). In a study conducted by Bower et al. (21), pain, depression and sleep disturbance strongly predicted fatigue group membership in breast cancer survivors. However, a number of studies also showed that the strong correlation between fatigue and depression does not mean it is a cause-effect relationship. The independence of fatigue from depression was shown in a study by Morrow (22) when cancer patients experiencing both fatigue and depression were treated with paroxetine and showed improvement only in their depressive symptoms. A recently completed longitudinal study showed that almost 1/3 of breast cancer survivors continue to experience significant fatigue 5-10 years after completion of treatment (23). The same study identified depressive symptoms as the strongest correlate and predictor of fatigue in breast cancer survivors.

Sleep problems are another commonly reported symptom among cancer patients. Studies of general cancer patient populations have reported elevated rates of insomnia throughout the course of the disease (24-32). There are few large-scale studies of the prevalence of sleep disturbance in cancer patients in the United States. A Canadian study of 982 general cancer patients found that the 31% had insomnia and 28% reported excessive sleepiness, with breast cancer patients having the highest prevalence of insomnia (33). Insomnia onset typically occurs either around the time of cancer

diagnosis or after cancer treatments. A prospective study of 170 early-stage breast cancer patients found that sleep problems predicted heightened distress two months and two years post-surgery (34). A study of 300 women with non-metastatic breast cancer who had received adjuvant therapy found that 19% had chronic, severe insomnia (35). In this study, onset of insomnia followed breast cancer diagnosis in 33% of the patients assessed. Breast cancer patients reporting significant sleep problems also report deficits in many areas of quality of life (36). A study of 50 breast cancer patients showed significant deterioration in quality of life related to impairments in sleep, physical activity, and social life (37). A recent study of 2,582 women treated for early stage breast cancer found that better physical health quality of life was associated with better sleep quality, and more physical activity (38). Better mental health quality of life was also associated with better sleep quality, fewer stressful life events, and less pain and fewer physical symptoms in this study. These results suggest that sleep quality influences daily functioning and quality of life among women with breast cancer. Sleep quality has a profound effect on the multiple compartments of the immune system, but particularly impacts upon levels of circulating cytokines (6, 7). Specifically, alterations in sleep either deprivation or improvements produce profound changes in proinflammatory cytokine such as TNF-alpha and IL-6, as well as levels of the inflammatory biomarker C-reactive protein (CRP). There is also provocative evidence that altered circadian rhythms may affect mortality in cancer. Circadian disruption across three consecutive days was prognostic of survival time in 104 patients with metastatic breast cancer up to seven years later, such that early mortality occurred among patients lacking a normal diurnal pattern (39). Increases in IFN-gamma and IL-1beta have also been observed along with sleep improvements among survivor of breast cancer (40). Although some initial associations between sleep quality and functional aspects of immunity have been observed, more research is needed in this area.

There is little research related to the experience of women prior to breast biopsy. Existing research suggests, however, that relationships exist between social support and symptom distress, coping, and quality of life throughout the breast cancer diagnosis and treatment trajectory.

What research exists suggests that pre-biopsy anxiety is associated with social support Seckel, M. M. and M. H. Birney (1996). "Social support, stress, and age in women undergoing breast biopsies." Clinical Nurse Specialist: The Journal for Advanced Nursing Practice 10(3): 137-143.

Social support is positively related to coping among women awaiting the results of breast biopsy. Drageset, S. and T. C. Lindstrom (2005). "Coping with a possible breast cancer diagnosis: demographic factors and social support." Journal of Advanced Nursing 51(3): 217-226. Recently diagnosed women who were less satisfied with emotional support from their family, friends and spouse are likely to experience difficulty in their interactions with nurses and physicians and to be less satisfied with their physicians. Han, W. T., K. Collie, et al. (2005). "Breast cancer and problems with medical interactions: relationships with traumatic stress, emotional self-efficacy, and social support." Psycho-Oncology 14(4): 318-330. The traumatic stress response in patients before surgery was related to social support. Tjemsland, L., J. A. Søreide, et al. (1996). "TRAUMATIC DISTRESS SYMPTOMS IN EARLY BREAST CANCER I: ACUTE RESPONSE TO DIAGNOSIS." Psycho-Oncology 5(1): 1-8.
Factors such as symptoms, coping, social support, and biochemical changes have been mentioned in the literature as potentially contributing to fatigue during adjuvant chemotherapy. Results have been conflicting and need further study. de Jong, N., A. M. Courtens, et al. (2002). "Fatigue in patients with breast cancer receiving adjuvant chemotherapy: a review of the literature." Cancer Nursing 25(4): 283-299.

Among Korean women receiving chemotherapy, Mood disturbance and social support had a significant interaction effect on symptom experience. A higher level of mood disturbance led to a higher level of symptoms when the level of social support was average or low Lee, E.-H., B. Y. Chung, et al. (2004). "Relationships of Mood Disturbance and Social Support to Symptom Experience in Korean Women with Breast Cancer." Journal of Pain and Symptom Management 27(5): 425-433.
Within the first two years following breast cancer surgery, social support from family members and friends helped to decrease the negative effects of symptoms on quality of life. Manning-Walsh, J. (2005). "Social support as a mediator between symptom distress and quality of life in women with breast cancer." JOGNN: Journal of Obstetric, Gynecologic, & Neonatal Nursing 34(4): 482-493.

B. Systemic Biomarkers

Biomarkers like carcinoembrionic antigen, CA-125 and prostate-specific antigen (PSA) are helpful in early detection and monitoring cancer (41). Three new serum biomarkers derived from membrane proteins found on breast cancer cells, Aminopeptidase N (CD13), membrane type 1-matrix metalloproteinase (MT1-MMP), and stromal derived receptor-1 (SDR-1), are hopeful novel biomarkers that may prove useful in the early detection of breast cancer. We are evaluating the presence of three novel biomarkers in newly diagnosed breast cancer.

Aminopeptidase N, also known as CD13, is a membrane-bound, zinc-dependent peptidase that cleaves neutral amino acids from the N terminus of oligopeptides. In addition to being expressed by a number of tissues, CD13 is aberrantly upregulated on both the tumor cells and developing blood vessels of cancerous tissue. Accumulating evidence points to CD13 as a key regulator in this tissue of both angiogenesis, or new blood vessel formation (42, 43), and the migration and invasion of tumor cells (44, 45). Interestingly, although CD13 was first defined as a membrane bound protein, a soluble form was later detected in a variety of bodily fluids including blood. Moreover, a number of studies have shown CD13 to be elevated in the serum of cancer patients, and to correlate with larger tumor size (46, 47).
Membrane type 1-matrix metalloproteinase (MT1-MMP) also shares similar characteristics as CD13. It is expressed as an inactive cell surface proteinase which is induced under breast cancer progression and angiogenic responses (48-50). Interestingly, the functional activation of MT1-MMP results in increased cell migration and invasion and has been shown to be actively translocated to the cell surface in hypoxia, both in vitro and in human breast cancer (51). It has also been shown to be shed from tumors as an active fragment which can be detected by MT1-MMP-specific fluorescent peptide substrates (52, 53).

The third biomarker is a novel cell surface protein which is over-expressed in human breast cancer and is selective for a highly invasive ductal carcinoma; high expression predicts distant metastasis (54). This cell surface protein also depicts cleaved protein isoforms in human breast tumor lysates indicating it may be shed in blood. This novel tumor antigen was identified from a breast cancer patient's sentinel lymph node and an antibody directed against it was synthesized. This unique antibody will be used in a fluorescent-based assay on blood samples to determine whether it is a potential diagnostic marker.

Purpose

This study will be a multidisciplinary analysis of distress and systemic biomarkers in patients referred for biopsy of a suspected breast cancer lesion. In recent years, early detection of breast cancer through screening mammography has helped to significantly improve clinical outcomes. Though the benefit of early detection by mammography is well established, a large percentage of patients referred for needle aspirate or core biopsies of a suspicious lesion are found to be cancer free; 75% at the University of Connecticut Health Center. Thus, the benefit to those with confirmed cancer comes at the expense of putting a number of women through a stressful and invasive procedure. More work is needed to understand the psychological effects of this event as well as search for less invasive methods of detecting the presence of cancer.

Little is known about the symptom experience of women anticipating diagnostic procedures such as breast biopsy. An understanding of the nature of the symptom experience of women with abnormal mammograms or clinical examination suggestive of breast cancer is necessary in order to plan interventions that are appropriate, acceptable, and effective in mitigating symptom distress and improving quality of life in this population.

Although much research has been done regarding the clinical benefits of screening, to date no studies have thoroughly evaluated the mental health and emotional costs of a suspect lesion. Depression, anxiety, insomnia and fatigue are all likely outcomes but rarely measured or investigated, and as a result there is little emotional support offered to these women. Social support is a possible moderator of these relationships.

Using available validated measures on a newly designed web-based survey, we will measure disturbances in sleep, fatigue, anxiety and depression in patients being evaluated for a palpable breast mass or abnormal mammogram. At the same time in the same patient population utilizing blood samples, we will measure levels of inflammatory markers in the serum of these patients to identify low-grade systemic inflammation and any potential relationship to distress, behavioral factors and fatigue, or probability of cancer. In addition, we will measure social support.

The probability of cancer will ultimately be determined by the biopsy outcome but the measurement of novel biomarkers in blood will be an attempt to define a rapid, less invasive measure of the presence of cancer. We have identified three protein antigens that are released from the surface of tumor cells and circulate in the blood noted in the background above. Although serum levels and activity of these molecules has been shown to correlate with presence and size of cancers in small pilot studies, a comprehensive evaluation of their utility as predictive biomarkers has not been performed. We propose to do this in this patient population. By obtaining a broad understanding of the health status of these patients, we hope to better understand the needs of this population and to identify potential areas for simple and specific intervention.

We will accomplish the symptom distress and biomarker research utilizing our Multidisciplinary Team, which includes the Departments of Psychology and Nursing at our Storrs campus, the Laboratory of Vascular Biology at the UCONN Health Sciences Center and our clinical faculty in the Neag Comprehensive Cancer Center.

Hypotheses:

1. Women who undergo evaluation for a suspect mammogram or palpable lesion will experience significant symptom distress including, fatigue, depression, anxiety and alterations in sleep. Poorer sleep quality, greater depressive and anxious symptoms and greater fatigue will be significantly associated with poorer quality of life. Extent of symptom distress will be moderated by social support

2. The levels of pro-inflammatory cytokines will correlate with the symptom distress experienced by these women.

3. One or more of the novel biomakers will be able to predict the presence of breast cancer at the time of biopsy.

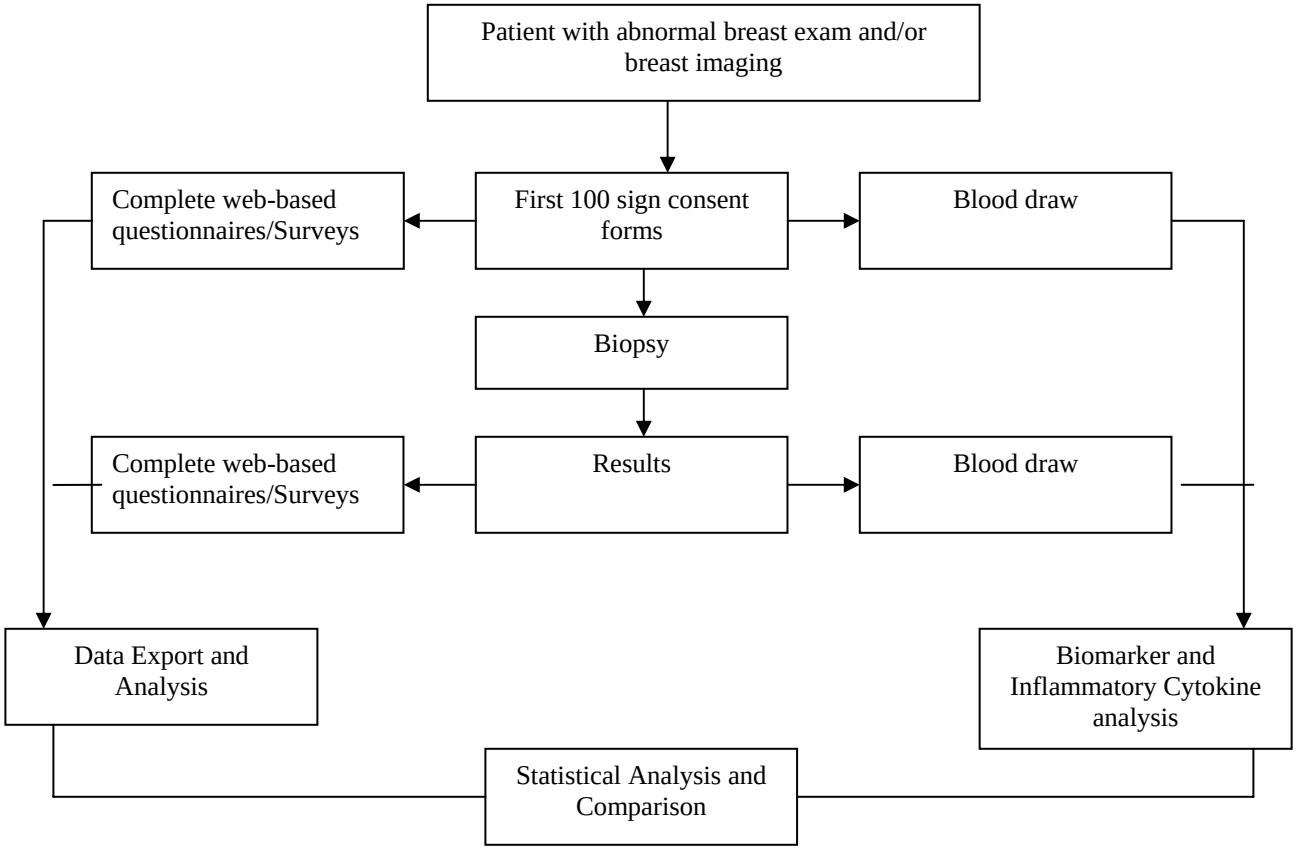
Specific Aims:

1. To measure the level of symptom distress (depression, anxiety, insomnia, fatigue) and social support experienced by women who have an abnormal physical exam or mammogram for which biopsy is recommended. Assessment will occur before and after biopsy, and we will examine the association of our symptom distress, social support, and quality of life measures. Symptom distress will be quantified before and after the biopsy to identify the impact of biopsy results on symptom distress.

2. To measure, before and after biopsy, the levels of pro-inflammatory cytokines and novel biomarkers (please refer to specific aim 3) to examine the association between these cytokine levels and our symptom distress outcomes.

3. We will measure, prior to biopsy, three new serum biomarkers derived from membrane proteins found on breast cancer cells, Aminopeptidase N (CD13), membrane type 1-matrix metalloproteinase (MT1-MMP), and stromal derived receptor-1 (SDR-1). We will evaluate their relationship to the biopsy outcome.

Study Schema:



Duration of the Study:

We plan to enroll 100 women in the study in one year's time.

Patient Eligibility and Ineligibility

Conditions for patient eligibility

1. Women who satisfy all of the following conditions are the only patients who will be eligible for this study.

2. The patient must consent to be in the study and must have signed an approved consent form conforming with federal and institutional guidelines.

3. Patients must be ≥ 18 years old.

4. Patients must have an abnormal breast imaging studies (ultrasound, mammogram, or MRI) and/or breast exam.

5. Patients with a history of *non-breast* malignancies are eligible if they have been disease-free for 5 or more years prior to randomization and are deemed by their physician to be at low risk for recurrence. Patients with the following cancers are eligible if diagnosed and treated within the past 5 years: carcinoma in situ

of the cervix, carcinoma in situ of the colon, melanoma in situ, and basal cell and squamous cell carcinoma of the skin.

6. Patients must not have been diagnosed with breast cancer prior to enrollment.

Conditions for patient ineligibility

1. The patient does not consent to be in the study.

2. Patients are < 18 years old.

3. Patients with a normal breast imaging and/or breast exam.

4. Patients diagnosed with breast cancer prior to enrollment.

Study Schedule:

Required studies	Prior to biopsy	After the biopsy
Breast assessment/exam/Patient Discussion	X	X
Blood Draw for Serum Collection/Biomarker	X	X
Panas Questionnaire	X	X
PSQI Questionniare	X	X
Hospital Anxiety and Depression Scale (HADS)	X	X
EORTC QOL	X	X
BFI for Fatigue	X	X
MOS Social Support Survey	X	X

Study Design and Methods:

One hundred patients who have either an abnormal breast imaging or breast exam and who have been sent to the surgeons of the Neag Comprehensive Cancer Center for evaluation will be enrolled into this study. Data from March 2005 to April 2006 showed from a pool of 402 breast biopsies were performed of which 27% were positive for invasive cancer and 6% for ductal carcinoma in situ. Thus, we expect to have a test pool of approximately 30 with cancer and 70 as control subjects. Informed consent will be obtained by the clinical personnel. We will obtain demographic, psychosocial and clinical information about the enrolled subjects. The demographic information will include race, ethnicity, age, marital status, employment and income level. Psychosocial information will include assessment of overall financial status and support from friends and family. Clinical information will include psychiatric and substance use history, family psychiatric and substance use history, medical history and medications. Symptom distress including specific measures for fatigue, depression and sleep and the patient's social support will be measured using well validated questionnaires including:

Assessment of Fatigue using Brief Fatigue Inventory (BFI) (55), Sleep disorders using Pittsburgh Sleep Quality Index (PSQI, 34) (56), Depression and anxiety using Hospital Anxiety and

Depression Scale (HADS) (57), Panas, quality of life using the European organization for research and treatment of cancer QLQ-30 (EORTC QOL) scale (58) and the MOS Social Support Survey (Sherbourne, C. D. and A. L. Stewart (1991). "The MOS social support survey." Social Science & Medicine **32**(6): 705-714.

). The questionnaires will be uploaded into a Web based survey that we have already developed with our information technology department. This will enable patients to answer these questionnaires at home if preferred, or in a consult office within the cancer center. We will request patients to complete them at the time of the patient's initial surgical consult for biopsy and after biopsy results are obtained. (See schema below). Blood samples will be collected from subjects at the inner elbow by venipuncture into Vacutainer Tubes. The biopsy results will be determined from the patient's pathology report and medical record chart, reflecting the ultrasound and sample diagnostic tests performed at the University of Connecticut Health Center.

Serum collection:

Timing of serum collections

Serum will be collected at the following timepoints:
• baseline *(prior to the patients biopsy)*; and
• after the patient's biopsy.

How the blood will be collected:

For the serum we will use two red top tubes and collect 20 mL of blood.

For the biomarkers we will use one red top tube and collect 10 mL of blood.

Specimen Processing

Samples will be centrifuged, serum collected and frozen at minus eighty degrees Celsius. The remainder of the sample will be discarded. As frozen samples have been shown to retain CD13 and MT1-MMP activity, sample analysis will be performed in batches. Two surrogate markers of the inflammatory state, C-reactive protein (CRP) and interleukin-6 (IL-6) will be measured in addition to the three novel biomarkers described earlier. Blood samples which are found to exhibit hemolysis will be discarded, as this will interfere with the colorimetric or fluorimetric assays.

Statistical Analysis:

In order to assure adequate power to test our main hypotheses, we propose to assess 100 patients. Before conducting the statistical tests of our hypotheses, we will evaluate a number of potentially confounding demographic, medical and health behavioral factors that might impact the associations under study. Specifically, we will examine whether demographic factors (e.g., age, ethnicity, income, education, etc.), medical status (e.g., current medical diagnoses, medication use, prior history of cancer, etc.) and health behaviors (e.g., alcohol, illicit drug, or cigarette use) are associated with our distress and pro-inflammatory measures. Any of these variables associated with our outcomes (at $p < .05$) will be controlled for in the subsequent main analyses.

Prior to our main analyses, we will also examine the distributions of all outcome variables under study and perform statistical transformations on those that are not normally distributed.

In our main analyses, we will examine the baseline association between our symptom distress measures (depression, anxiety, insomnia, and fatigue) and our pro-inflammatory cytokine measures using correlational analyses, while controlling for relevant demographic, medical and health behavior variables. To identify the moderating role of social support, we will use hierarchical regression. To examine the association between these measures over time in the entire sample, we will utilize residualized change scores which allow us to examine the association between the distress and pro-inflammatory cytokine measures, while control for baseline values of each of the outcome measures. To quantify differences in distress and pro-inflammatory cytokines between those women having a positive biopsy versus those having a negative biopsy will using utilize a 2x2 repeated measures ANOVA with biopsy status (positive or negative) as the between subjects factor and time (pre and post-biopsy) as the within subjects factor. All data analyses will be performed using SPSS version 13.0. All statistical tests will be carried out at a two-sided alpha = .05.

Protection of Human Subjects:

1. Risks to the Subjects

a. Human Subjects Involvement and Characteristics

This project involves the collection of a single blood sample from each patient and the collection of information regarding each patient's clinical status. The patient population will be drawn from breast cancer patients of the University of Connecticut Neag Comprehensive Cancer Center in Farmington, Connecticut. This target population consists of women, 20-80 years of age, and our target enrollment is 100. Control subjects will be drawn from the population of patients with negative results from the biopsy of a suspected cancerous lesion.

b. Sources of Material

A single blood sample, specifically for use in this research project, will be collected from each patient, and data pertaining to her cancer will be collected from her chart. All specimen and clinical data will be stored with physical and password security to which only the PI will have access. A random number will be used in maintaining research results on blood specimens, and connecting research results to clinical patient information. According to the HIPPA agreement signed by each subject, protected health information may be shared with The University of Connecticut Health Center's Institutional Review and the Office of Research Compliance; Government representatives, when required by law; Hospital or University of Connecticut Health Center representatives; or University of Connecticut Health Center research collaborators with Institutional Review Board approved Protocols.

c. Potential Risks

The risks associated with this study correspond to the mild risks associated with a routine blood draw. Occasionally, subjects may feel light-headed or experience bruising at the site where blood was taken. Although rare, it is also possible that they might experience excessive bleeding, or develop an infection. Appropriate safety precautions will be taken to minimize these risks. The information obtained as a result of this study is not expected to affect the patient under study, and no attempt will be made to contact the patient regarding the results.

The initial interview and study questionnaires may address potentially sensitive matters such as psychiatric symptoms, medical condition, and other problems. Study participants may feel some emotional distress or discomfort during discussion of these issues.

2. Adequacy of Protection Against Risks

a. Recruitment and Informed Consent
Consent will be obtained by Susan Tannenbaum, M.D. or her staff in the Neag Comprehensive Cancer Center at the University of Connecticut Health Center in Farmington, CT. The consent form will be presented to subjects who are visiting the office for biopsy of a suspected cancerous lesion. Subjects will be allowed to consent, by signature, to enter the study during that same visit. All efforts will be made to ensure that the individuals are fully informed, understand the materials provided to them, and are competent to provide consent. In the case of subjects with limited decision-making capacity, language barriers or hearing difficulties, subjects will be asked to explain the purpose and procedures of the study as well as the benefits and risks. If it is determined that the subject is incapable of providing consent, consent will be sought from the subject's legal guardian.

b. Protection Against Risk
Although confidentiality cannot be 100% guaranteed, efforts will be made to maintain the confidentiality of each participant. As mentioned, all specimen and clinical data will be stored with physical and password security to which only the PI will have access, and a random number will be used in maintaining research results on blood specimens and connecting research results to clinical patient information. In the event of an adverse effect, such as an infection at the site of venipuncture, the staff of John Dempsey Hospital at the University of Connecticut Health Center will provide appropriate treatment.

Concerning the possibility of psychological distress related to study interview and assessments, subjects will be allowed to take a break during these assessments if needed. Also, subjects will be informed through the informed consent process that they can withdraw from the study at any time.

3. Potential Benefits Of The Proposed Research To The Subjects And Others

For each individual participant, for whom there is no direct benefit from this study, there maybe an increased ratio of risks to benefits. For society as a whole, however, the mild risks associated with a blood draw, weighted against the significant benefits of knowledge gained, makes the ratio of risks to benefits small. Additionally , women given an opportunity to address and define their symptoms of distress may gain benefit from the process alone.

4. Importance of The Knowledge To Be Gained

The knowledge to be gained from this study may lead to the establishment of new serum biomarkers for breast cancer which would be useful in the diagnosis of breast cancer. This study will improve our understanding of symptom distress experienced by women referred for biopsy of a suspected breast cancer lesion.

Inclusion of Women and Minorities

This study will be restricted to subjects of the female gender because of the nature of the disease. There will be no selection bias according to race or ethnicity. Since subjects will not be specifically recruited for this study, the race and ethnicity of the subjects enrolled will likely reflect the profile of patients which currently seek care for their cancer at the Neag Comprehensive Cancer Center of the University of Connecticut.

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